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STIC Database Tracking Number: 97806

TO: Jennifer Kim **Location: 2d17 / 2b19** **Tuesday, July 01, 2003** **Art Unit: 1617** **Phone: 308-2232** **Serial Number: 09 / 719770**	**From: Jan Delaval** **Location: Biotech-Chem Library** **CM1-1E07** **Phone: 308-4498** **jan.delaval@uspto.gov**

Search Notes

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

Jan Delaval

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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jennifer Kim Examiner #: 77469 Date: 7/1/03
Art Unit: 1617 Phone Number 30 8-2232 Serial Number: 09/719770
Mail Box and Bldg/Room Location: 2D17 Results Format Preferred (circle): PAPER DISK E-MAIL
2B19

If more than one search is submitted, please prioritize searches in order of need. MEJ

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Methods + Compositions for treating diseases mediated by transglutaminase activity

Inventors (please provide full names): Laurence Steinman

Earliest Priority Filing Date: 6/17/98

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

1) Please search claims 1-3, 15+16 based on the disease listed in claim 3 with active agent of claim 8 of Monodansyl cadaverine!!

2) Please provide registry # of ↑

THX,

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

****

STAFF USE ONLY

STIC SEARCH RESULTS

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact:***

Mary Hale, Information Branch Supervisor
308-4258, CM1-1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

  Types of relevant prior art found:
  - ☐ Foreign Patent(s)
  - ☐ Non-Patent Literature
    (journal articles, conference proceedings, new product announcements etc.)
- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk

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FILE LAST UPDATED: 30 Jun 2003 (20030630/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

Jan Delaval
Reference Librarian
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jan.delaval@uspto.gov

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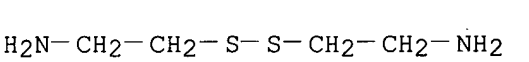
L71 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:224182 HCAPLUS
TI Prolonged survival and decreased abnormal movements in transgenic model of **Huntington** disease, with administration of the **transglutaminase** Inhibitor cystamine. [Erratum to document cited in CA137:592]
AU Karpuj, Marcela V.; Becher, Mark W.; Springer, Joe E.; Chabas, Dorothee; Youssef, Sawsan; Pedotti, Rosetta; Mithcell, Dennis; **Steinman, Lawrence**
CS Department of Neurological Sciences, Stanford University, Stanford, CA, USA
SO Nature Medicine (New York, NY, United States) (2002), 8(3), 303
CODEN: NAMEFI; ISSN: 1078-8956
PB Nature America Inc.
DT Journal; Errata
LA English
CC 1-11 (Pharmacology)
AB An erratum.
ST erratum **transglutaminase** inhibitor cystamine **Huntington** disease huntingtin polyglutamine; **transglutaminase** inhibitor cystamine **Huntington** disease huntingtin polyglutamine erratum
IT INDEXING IN PROGRESS
IT **Nervous system**
(**Huntington's chorea; transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease (Erratum))
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dnaj; **transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease in relation to transcription of (Erratum))
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(huntingtin; **transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease involving exon 1 of huntingtin contg. an expanded polyglutamine repeat (Erratum))

IT **51-85-4**, Cystamine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease (Erratum))
IT INDEXING IN PROGRESS
IT **51-85-4**, Cystamine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease (Erratum))
RN 51-85-4 HCAPLUS
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)



L71 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:123990 HCAPLUS
DN 137:592
TI Prolonged survival and decreased abnormal movements in transgenic model of **Huntington** disease, with administration of the **transglutaminase** inhibitor cystamine
AU Karpuj, Marcela V.; Becher, Mark W.; Springer, Joe E.; Chabas, Dorothee; Youssef, Sawsan; Pedotti, Rosetta; Mitchell, Dennis; **Steinman, Lawrence**
CS Department of Neurological Sciences, Stanford University, Stanford, CA, USA
SO Nature Medicine (New York, NY, United States) (2002), 8(2), 143-149
CODEN: NAMEFI; ISSN: 1078-8956
PB Nature America Inc.
DT Journal
LA English
CC 1-11 (Pharmacology)
AB An expanded polyglutamine domain in huntingtin underlies the pathogenic events in **Huntington** disease (HD), characterized by **chorea**, dementia and severe wt. loss, culminating in death. **Transglutaminase** (TGase) may be crit. in the pathogenesis, via crosslinking huntingtin. Administration of the TGase competitive inhibitor cystamine to transgenic mice expressing exon 1 of huntingtin contg. an expanded polyglutamine repeat, altered the course of their HD-like disease. Cystamine given i.p. entered the brain, where it inhibited TGase activity. When treatment was begun after the appearance of abnormal movements, cystamine extended survival, reduced the assocd. tremor and abnormal movements and ameliorated wt. loss. Treatment did not influence the appearance or frequency of neuronal nuclear inclusions. Unexpectedly, cystamine increased transcription of one of the two genes shown to be neuroprotective for polyglutamine toxicity in Drosophila, dnaj (also known as HD/1 and Hsp40 in humans and mice, resp.). Inhibition of TGase provides a new treatment strategy for HD and other polyglutamine diseases.
ST **transglutaminase** inhibitor cystamine **Huntington** disease huntingtin polyglutamine
IT **Nervous system, disease**
(**Huntington's chorea**; **transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(dnaj; **transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease in relation to transcription of)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(huntingtin; **transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease involving exon 1 of huntingtin contg. an expanded polyglutamine repeat)

IT **80146-85-6**, **Transglutaminase**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; **transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease)

IT **51-85-4**, Cystamine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease)

IT **26700-71-0**, Polyglutamine **69864-43-3**, Polyglutamine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease involving exon 1 of huntingtin contg. an expanded polyglutamine repeat)

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bates, G; Brain Pathol 1998, V8, P699 HCAPLUS
(2) Becher, M; Neurobiol Disease 1998, V4, P387 HCAPLUS
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(6) Cooper, A; J Neurochem 1997, V69, P431 HCAPLUS
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(11) Ferrante, R; J Neurosci 2000, V20, P4389 HCAPLUS
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(13) Folk, J; Biochim Biophys Acta 1966, V122, P244 HCAPLUS
(14) Green, H; Cell 1993, V74, P955 HCAPLUS
(15) Huang, C; Somatic Cell Mol Genet 1998, V24, P217 HCAPLUS
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(20) Kahlem, P; Mol Cell 1998, V1, P595 HCAPLUS
(21) Karpuj, M; Proc Natl Acad Sci 1999, V96, P7388 HCAPLUS
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(44) Voehringer, D; Proc Natl Acad Sci 2000, V97, P2680 HCAPLUS
(45) Yamamoto, A; Cell 2000, V101, P57 HCAPLUS
(46) Yu, S; Science 1999, V284, P336 HCAPLUS
(47) Zainelli, G; Soc Neurosci Absracts 2000, V26, P1297

IT **80146-85-6, Transglutaminase**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; **transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **51-85-4**, Cystamine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease)
RN 51-85-4 HCAPLUS
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)

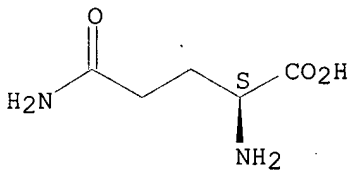
$H_2N-CH_2-CH_2-S-S-CH_2-CH_2-NH_2$

IT **26700-71-0**, Polyglutamine **69864-43-3**, Polyglutamine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**transglutaminase** inhibitor cystamine effect on survival and abnormal movements in a transgenic model of **Huntington** disease involving exon 1 of huntingtin contg. an expanded polyglutamine repeat)
RN 26700-71-0 HCAPLUS
CN L-Glutamine, homopolymer (9CI) (CA INDEX NAME)

CM 1

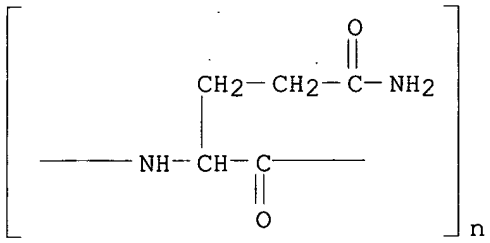
CRN 56-85-9
CMF C5 H10 N2 O3

Absolute stereochemistry.



RN 69864-43-3 HCAPLUS
CN Poly[imino[(1S)-1-(3-amino-3-oxopropyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA

INDEX NAME)



L71 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:811104 HCAPLUS
DN 132:45002
TI Methods and compositions for treating diseases mediated by **transglutaminase** activity
IN **Steinman, Lawrence**; Karpuj, Marcella V.
PA **Yeda Research and Development Co. Ltd., Israel**
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-48
ICS A61K031-13
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9965516	A1	19991223	WO 1999-US13615	19990617 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9948239	A1	20000105	AU 1999-48239	19990617 <--
PRAI US 1998-89603P	P	19980617 <--		
WO 1999-US13615	W	19990617 <--		

AB Diseases mediated by **transglutaminase**, e.g. **Huntington's** Disease, **spinobulbar atrophy**, **spinocerebellar ataxia**, and **dentatorubralpallidoluysian atrophy**, as well as inflammatory diseases of the central nervous system, including multiple sclerosis, rheumatoid arthritis, and insulin-dependent diabetes mellitus, can be treated by administering a **transglutaminase** inhibitor, e.g. **monodansyl cadaverine**, monoamines and diamines such as cystamine or putrescine, etc.
ST **transglutaminase** inhibitor therapeutic; nervous system disease **transglutaminase** inhibitor; antiinflammatory antidiabetic **transglutaminase** inhibitor
IT **Nervous system**
(**Huntington's chorea; transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)
IT Virus vectors

(and transkaryotic implantation; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Disease, animal
(**atrophy, spinobulbar; transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Encephalomyelitis
(autoimmune; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Erythrocyte
Erythrocyte
(cell membrane, liposome hybrid; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Autoimmune disease
(cell-mediated; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Nervous system
(central, inflammation; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Brain
(cerebellum; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Brain
(cortex; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Brain
(corticular nuclear ext.; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Nervous system
(degeneration; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT **Brain, disease**
(**dentatorubral-pallidoluysian atrophy; transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Cell membrane
Cell membrane
(erythrocyte, liposome hybrid; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(huntingtin; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Drug delivery systems
(immunoliposomes; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Diabetes mellitus
(insulin-dependent; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Drug delivery systems

(liposomes; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Aggregation
(of **polyQ**-contg. proteins; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(receptor-mediated gene delivery; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT **Nervous system**
(**spinocerebellar ataxia; transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Multiple sclerosis
(therapeutic agents; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Anti-inflammatory agents
Antidiabetic agents
Antirheumatic agents
Drug delivery systems
Gene therapy
Lymphoblast
Nervous system agents
Retroviral vectors
(**transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Antisense DNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**transglutaminase; transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT **24991-23-9 25513-46-6**, Polyglutamic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**polyQ**-contg. protein aggregation; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT **51-85-4**, Cystamine **64-77-7**, Tolbutamide **110-60-1**, Putrescine **150-13-0 616-34-2**, Glycine methyl ester **7758-98-7**, Cupric sulfate, biological studies **10121-91-2**, **Monodansyl cadaverine 74389-76-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT **80146-85-6, Transglutaminase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT 252868-73-8, 2: PN: WO9965516 SEQID: 3 unclaimed DNA 252868-74-9, 3: PN:

WO9965516 SEQID: 4 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT 252874-67-2
RL: PRP (Properties)
(unclaimed protein sequence; methods and compns. for treating diseases mediated by **transglutaminase** activity)

IT 252769-79-2
RL: PRP (Properties)
(unclaimed sequence; methods and compns. for treating diseases mediated by **transglutaminase** activity)

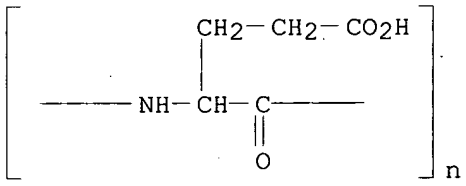
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Heska Corporation USA; WO 9824887 A2 1998 HCAPLUS
(2) O'Hara; US 5514579 A 1996 HCAPLUS
(3) Victoria University of Manchester; WO 9804245 A1 1998 HCAPLUS

IT **24991-23-9 25513-46-6**, Polyglutamic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**polyQ**-contg. protein aggregation; **transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

RN 24991-23-9 HCAPLUS
CN Poly[imino[(1S)-1-(2-carboxyethyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)

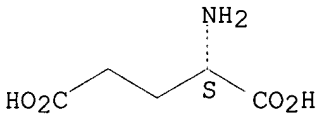


RN 25513-46-6 HCAPLUS
CN L-Glutamic acid, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 56-86-0
CMF C5 H9 N O4

Absolute stereochemistry.

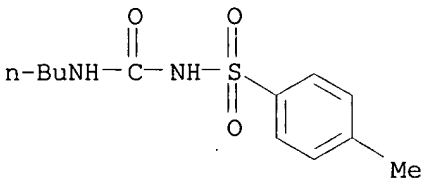


IT **51-85-4**, Cystamine **64-77-7**, Tolbutamide **110-60-1**, Putrescine **150-13-0 616-34-2**, Glycine methyl ester **7758-98-7**, Cupric sulfate, biological studies **10121-91-2**, **Monodansyl cadaverine 74389-76-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)

RN 51-85-4 HCAPLUS
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-S-S-CH_2-CH_2-NH_2$

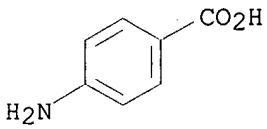
RN 64-77-7 HCAPLUS
CN Benzenesulfonamide, N-[(butylamino)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



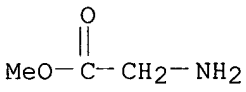
RN 110-60-1 HCAPLUS
CN 1,4-Butanediamine (8CI, 9CI) (CA INDEX NAME)

$H_2N-(CH_2)_4-NH_2$

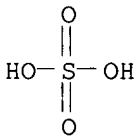
RN 150-13-0 HCAPLUS
CN Benzoic acid, 4-amino- (9CI) (CA INDEX NAME)



RN 616-34-2 HCAPLUS
CN Glycine, methyl ester (6CI, 8CI, 9CI) (CA INDEX NAME)



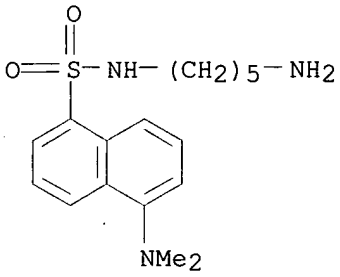
RN 7758-98-7 HCAPLUS
CN Sulfuric acid copper(2+) salt (1:1) (8CI, 9CI) (CA INDEX NAME)



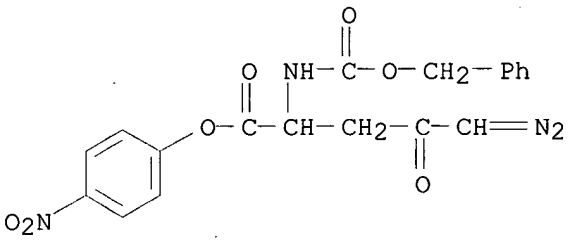
Cu(II)

RN 10121-91-2 HCAPLUS
CN 1-Naphthalenesulfonamide, N-(5-aminopentyl)-5-(dimethylamino)- (8CI, 9CI)

(CA INDEX NAME)



RN 74389-76-7 HCAPLUS
CN Norvaline, 5-diazo-4-oxo-N-[(phenylmethoxy)carbonyl]-, 4-nitrophenyl ester (9CI) (CA INDEX NAME)



IT **80146-85-6, Transglutaminase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**transglutaminase** inhibitor-based methods and compns. for treating diseases mediated by **transglutaminase** activity)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

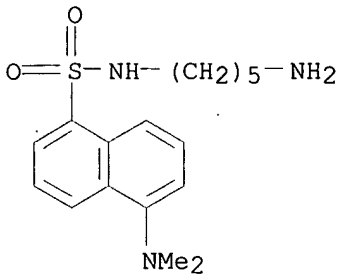
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L71 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:481278 HCAPLUS
DN 131:125479
TI Therapeutic agents for CAG repeat expansion disease
IN Tsuji, Shoji
PA Niigata University, Japan
SO Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K045-00
ICS A61K045-00; A61K031-195; A61K038-00
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 11209304	A2	19990803	JP 1998-27739	19980126 <--
	JP 3012923	B2	20000228		
	AU 9913191	A1	19990812	AU 1999-13191	19990122 <--
	US 6355690	B1	20020312	US 1999-236002	19990122 <--
	EP 950406	A2	19991020	EP 1999-101063	19990125 <--
	EP 950406	A3	20001129		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
CA 2260311 C 20021217 CA 1999-2260311 19990125 <--
PRAI JP 1998-27739 A 19980126 <--
AB Therapeutic agents for CAG repeat expansion disease comprise **transglutaminase** inhibitors i.e. cysteamine and **monodansyl cadaverine**. CAG repeat expansion disease is spinal and bulbar muscular **atrophy**, **Huntington**'s disease, spinocerebeller **ataxia** type 2, hereditary **dentatorubral pallidoluysian atrophy**, Machado-Joseph disease or autosomal dominal cerebellar **ataxia**.
ST CAG repeat expansion disease **transglutaminase** inhibitor; cysteamine CAG repeat expansion disease; **monodansyl cadaverine** CAG repeat expansion disease
IT Disease, animal
(CAG repeat expansion; therapeutic agents for CAG repeat expansion disease)
IT **Nervous system**
(**Huntington**'s **chorea**; therapeutic agents for CAG repeat expansion disease)
IT Nervous system
(Machado-Joseph disease; therapeutic agents for CAG repeat expansion disease)
IT Nervous system
(**ataxia**, spinocerebeller or autosomal dominal cerebellar; therapeutic agents for CAG repeat expansion disease)
IT Disease, animal
(**atrophy**, hereditary **dentatorubral pallidoluysian**; therapeutic agents for CAG repeat expansion disease)
IT Spinal muscular **atrophy**
(spinal and bulbar muscular **atrophy**; therapeutic agents for CAG repeat expansion disease)
IT **80146-85-6, Transglutaminase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; therapeutic agents for CAG repeat expansion disease)
IT 60-23-1, Cysteamine **10121-91-2, Monodansyl cadaverine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agents for CAG repeat expansion disease)
IT **80146-85-6, Transglutaminase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; therapeutic agents for CAG repeat expansion disease)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **10121-91-2, Monodansyl cadaverine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agents for CAG repeat expansion disease)
RN 10121-91-2 HCAPLUS
CN 1-Naphthalenesulfonamide, N-(5-aminopentyl)-5-(dimethylamino)- (8CI, 9CI) (CA INDEX NAME)



L71 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:406389 HCAPLUS
DN 129:79862
TI CAG repeat diseases and neuronal cell death
AU Igarashi, Shuichi; Koide, Reiji; Shimohata, Takayoshi; Tsuji, Shoji
CS Brain Res. Inst., Niigata Univ., Niigata, 951, Japan
SO Jikken Igaku (**1998**), 16(10), 1277-1280
CODEN: JIIGEF; ISSN: 0288-5514
PB Yodosha
DT Journal; General Review
LA Japanese
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
AB A review with 10 refs., on involvement of aggregates of proteins contg. polyglutamine in mechanisms of CAG repeat diseases (Huntington's disease, Machado-Joseph disease, **dentatorubral**-pallidoluysian atrophy, etc.) and neuronal cell death. Involvement of **transglutaminase** in aggregate formation is also discussed.
ST review CAG repeat disease polyglutamine aggregation; neuronal cell death polyglutamine aggregation review; **transglutaminase** polyglutamine aggregation neuronal cell review
IT Nerve, disease
(death; involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)
IT Nervous system
(degeneration; involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)
IT Mutation
(expansion; involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)
IT Repetitive DNA
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)
IT Cell death
(neuron; involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)
IT **80146-85-6, Transglutaminase**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)
IT **26700-71-0**, Polyglutamine **69864-43-3**, Polyglutamine
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)

IT **101985-79-9**, DCAG
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (repeat; involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)

IT **80146-85-6, Transglutaminase**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)

RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

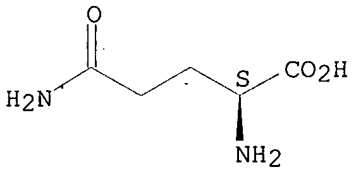
IT **26700-71-0**, Polyglutamine **69864-43-3**, Polyglutamine
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)

RN 26700-71-0 HCAPLUS
CN L-Glutamine, homopolymer (9CI) (CA INDEX NAME)

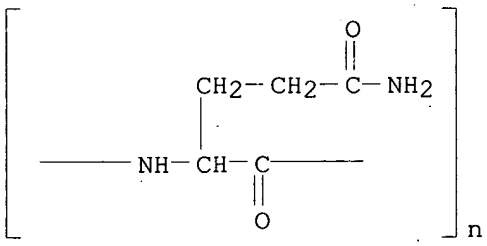
CM 1

CRN 56-85-9
CMF C5 H10 N2 O3

Absolute stereochemistry.



RN 69864-43-3 HCAPLUS
CN Poly[imino[(1S)-1-(3-amino-3-oxopropyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)

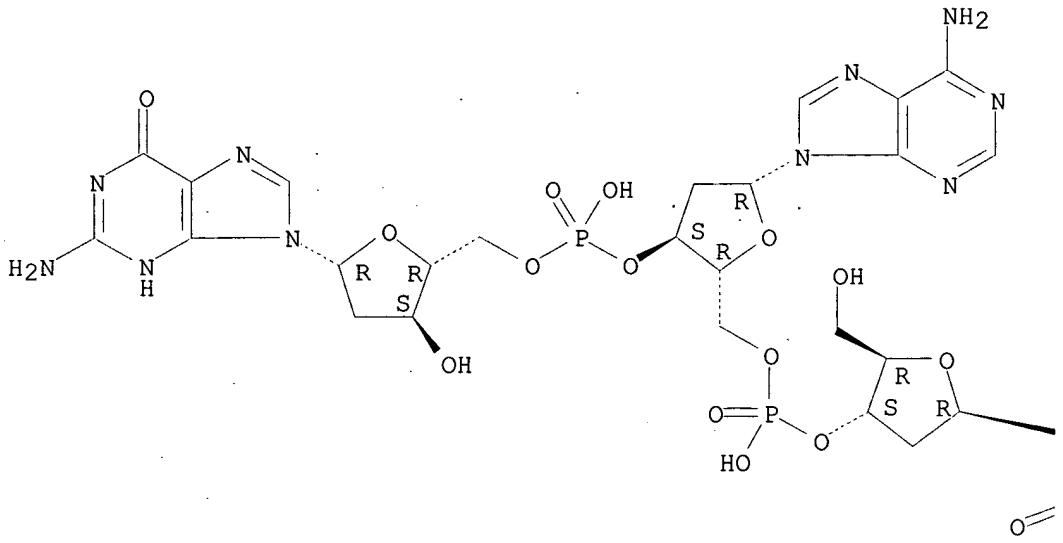


IT **101985-79-9**, DCAG
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (repeat; involvement of polyglutamine aggregation in CAG repeat diseases and neuronal cell death)

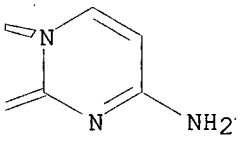
RN 101985-79-9 HCAPLUS
CN Guanosine, 2'-deoxycytidylyl-(3'.fwdarw.5')-2'-deoxyadenylyl-(3'.fwdarw.5')-2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L71 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:272230 HCAPLUS
DN 129:53015
TI Tissue **transglutaminase**-catalyzed formation of high-molecular-weight aggregates in vitro is favored with long polyglutamine domains: a possible mechanism contributing to CAG-triplet diseases
AU Gentile, Vittorio; Sepe, Carlo; Calvani, Menotti; Melone, Mariarosa A. B.; Cotrufo, Roberto; Cooper, Arthur J. L.; Blass, John P.; Peluso, Gianfranco
CS Dipartimento di Biochimica e Biofisica, Seconda Universita di Napoli, Naples, 80138, Italy
SO Archives of Biochemistry and Biophysics (**1998**), 352(2), 314-321

CODEN: ABBIA4; ISSN: 0003-9861
PB Academic Press
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
AB To investigate possible biochem. mechanisms underlying the "toxic gain of function" assocd. with polyglutamine expansions, the ability of guinea pig liver tissue **transglutaminase** to catalyze covalent attachments of various polyamines to polyglutamine peptides was examd. Of the polyamines tested, spermine is the most active substrate, followed by spermidine and putrescine. Formation of covalent crosslinks between polyglutamine peptides and polyamines yields high-Mr aggregates - a process that is favored with longer polyglutamines. In the presence of tissue **transglutaminase**, purified glyceraldehyde-3-phosphate dehydrogenase (a key glycolytic enzyme that binds tightly to the polyglutamine domains of both huntingtin and **dentatorubral-pallidoluysian atrophy** proteins) is covalently attached to polyglutamine peptides in vitro, resulting in the formation of high-Mr aggregates. In addn., endogenous glyceraldehyde-3-phosphate dehydrogenase of a Balb-c 3T3 fibroblast cell line overexpressing human tissue **transglutaminase** forms crosslinks with a Q60 polypeptide added to the cell homogenate. Possibly, expansion of polyglutamine domains (thus far known to occur in the gene products assocd. with at least seven neurodegenerative diseases) leads to increased/aberrant tissue **transglutaminase**-catalyzed crosslinking reactions with both polyamines and susceptible proteins, such as glyceraldehyde-3-phosphate dehydrogenase. Formation of crosslinked heteropolymers may lead to deposition of high-Mr protein aggregates, thereby contributing to cell death.
ST polyglutamine protein crosslinking aggregation CAG disease; CAG triplet disease polyglutamine protein crosslinking
IT Crosslinking
(biol.; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)
IT Nervous system
(degeneration; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)
IT Mutation
(expansion, of CAG trinucleotide repeat; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)
IT Disease, animal
(genetic, trinucleotide repeat; tissue **transglutaminase** -catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)
IT Amines, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(polyamines, nonpolymeric, crosslinking; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)
IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);

BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(polyglutamine-contg.; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

IT Repeat motifs (protein)
(polyglutamine; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

IT Cell death
Molecular association
(tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

IT Repetitive DNA
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(trinucleotide; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

IT 71-44-3, Spermine **110-60-1**, Putrescine 124-20-9, Spermidine 9001-50-7, Glyceraldehyde-3-phosphate dehydrogenase
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(crosslinking; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

IT **80146-85-6**, Glutaminylpeptide .gamma.-glutamyltransferase
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

IT **26700-71-0D**, Polyglutamine, proteins contg. **69864-43-3D**, Polyglutamine, proteins contg.
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

IT **101985-79-9**, d-CAG
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **110-60-1**, Putrescine
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(crosslinking; tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

RN 110-60-1 HCAPLUS
CN 1,4-Butanediamine (8CI, 9CI) (CA INDEX NAME)

$H_2N-(CH_2)_4-NH_2$

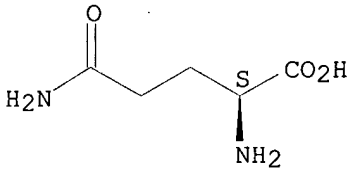
IT **80146-85-6**, Glutaminylpeptide .gamma.-glutamyltransferase
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **26700-71-0D**, Polyglutamine, proteins contg. **69864-43-3D**, Polyglutamine, proteins contg.
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)
RN 26700-71-0 HCAPLUS
CN L-Glutamine, homopolymer (9CI) (CA INDEX NAME)

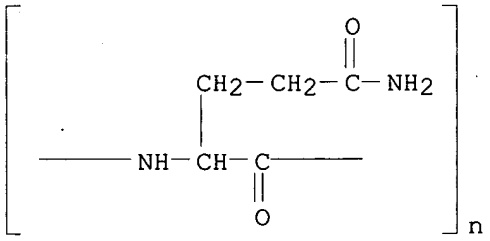
CM 1

CRN 56-85-9
CMF C5 H10 N2 O3

Absolute stereochemistry.



RN 69864-43-3 HCAPLUS
CN Poly[imino[(1S)-1-(3-amino-3-oxopropyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



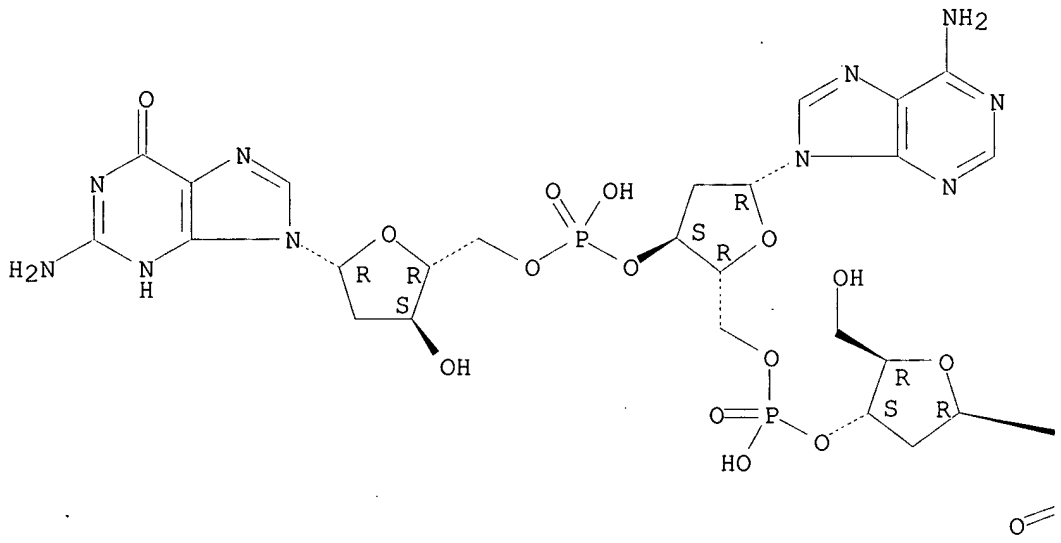
IT **101985-79-9**, d-CAG
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU

(Occurrence)
(tissue **transglutaminase**-catalyzed formation of high-mol.-wt. aggregates in vitro is favored with long polyglutamine domains: possible mechanism contributing to human CAG-triplet neurodegenerative diseases)

RN 101985-79-9 HCAPLUS
CN Guanosine, 2'-deoxycytidylyl-(3'.fwdarw.5')-2'-deoxyadenylyl-(3'.fwdarw.5')-2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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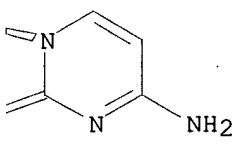

L71 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:225134 HCAPLUS

DN 129:3545
TI **Transglutaminase** action imitates **Huntington**'s disease: selective polymerization of huntingtin containing expanded polyglutamine
AU Kahlem, Pascal; Green, Howard; Djian, Philippe
CS Centre National de la Recherche Scientifique, Centre de Recherche sur l'Endocrinologie Moleculaire et le Developpement, Meudon-Bellevue, 92190, Fr.
SO Molecular Cell (**1998**), 1(4), 595-601
CODEN: MOCEFL; ISSN: 1097-2765
PB Cell Press
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
AB Different proteins bearing polyglutamine of excessive length are lethal to neurons and cause human disease of the central nervous system. In parts of the brain affected by **Huntington**'s disease, the amt. of the huntingtin with expanded polyglutamine is reduced and there appear huntingtin-contg. polymers of larger mol. wt. We show here that huntingtin is a substrate of **transglutaminase** in vitro and that the rate const. of the reaction increases with length of the polyglutamine over a range of an order of magnitude. As a result, huntingtin with expanded polyglutamine is preferentially incorporated into polymers. Both disappearance of the huntingtin with expanded polyglutamine and its replacement by polymeric forms are prevented by inhibitors of **transglutaminase**. The effect of **transglutaminase** therefore duplicates the changes in the affected parts of the brain.
ST **Huntington** disease huntingtin polyglutamine **transglutaminase**
IT **Nervous system**
(**Huntington**'s **chorea**; **transglutaminase** action imitates **Huntington**'s disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)
IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(huntingtins; **transglutaminase** action imitates **Huntington**'s disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)
IT Disease models
(**transglutaminase** action imitates **Huntington**'s disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)
IT **80146-85-6**, **Transglutaminase**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**transglutaminase** action imitates **Huntington**'s disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)
IT **26700-71-0**, Polyglutamine **69864-43-3**, Polyglutamine
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**transglutaminase** action imitates **Huntington**'s disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)
IT **51-85-4**, Cystamine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**transglutaminase** action imitates **Huntington**'s disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)

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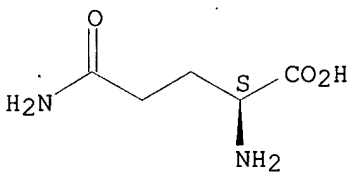
IT **80146-85-6, Transglutaminase**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**transglutaminase** action imitates **Huntington's** disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **26700-71-0**, Polyglutamine **69864-43-3**, Polyglutamine
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**transglutaminase** action imitates **Huntington's** disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)
RN 26700-71-0 HCAPLUS
CN L-Glutamine, homopolymer (9CI) (CA INDEX NAME)

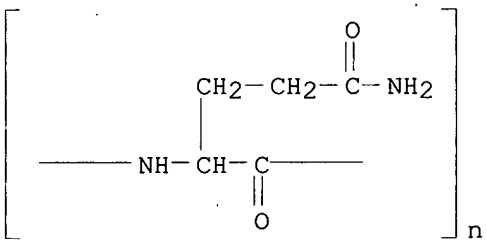
CM 1

CRN 56-85-9
CMF C5 H10 N2 O3

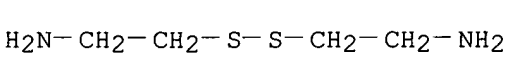
Absolute stereochemistry.



RN 69864-43-3 HCAPLUS
CN Poly[imino[(1S)-1-(3-amino-3-oxopropyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



IT **51-85-4**, Cystamine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**transglutaminase** action imitates **Huntington**'s disease by inducing selective polymn. of huntingtin contg. expanded polyglutamine)
RN 51-85-4 HCAPLUS
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)



L71 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:85454 HCAPLUS
DN 128:179041
TI Suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with an expanded polyglutamine stretch
AU Igarashi, Shuichi; Koide, Reiji; Shimohata, Takayoshi; Yamada, Mitsunori; Hayashi, Yasuko; Takano, Hiroki; Date, Hidetoshi; Oyake, Mutsuo; Sato, Toshiya; Sato, Aki; Egawa, Shigekimi; Ikeuchi, Takeshi; Tanaka, Hajime; Nakano, Ryoichi; Tanaka, Keiko; Hozumi, Isao; Inuzuka, Takashi; Takahashi, Hitoshi; Tsuji, Shoji
CS Dep. Neurology, Niigata Univ., Niigata, 1-757, Japan
SO Nature Genetics (**1998**), 18(2), 111-117
CODEN: NGENEC; ISSN: 1061-4036
PB Nature America
DT Journal
LA English
CC 14-14 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1, 3
AB To elucidate the mol. mechanisms whereby expanded polyglutamine stretches elicit a grain of toxic function, we expressed full-length and truncated DRPLA (**dentatorubral-pallidoluysian atrophy**)

cDNAs with or without expanded CAG repeats in COS-7 cells. We found that truncated DRPLA proteins contg. an expanded polyglutamine stretch form filamentous peri- and intranuclear aggregates and undergo apoptosis. The apoptotic cell death was partially suppressed by the **transglutaminase** inhibitors cystamine and **monodansyl cadaverine** (but not putrescine), suggesting involvement of a **transglutaminase** reaction and providing a potential basis for the development of therapeutic measures for CAG-repeat expansion diseases.

ST DRPLA protein **transglutaminase** inhibitor apoptosis; CAG repeat DRPLA protein cytotoxicity; **dentatorubral pallidoluysian atrophy**

IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(DRPLA (**dentatorubral-pallidoluysian atrophy**); suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)

IT **Brain, disease**
(**dentatorubral-pallidoluysian atrophy**; suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)

IT Apoptosis
(suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)

IT Repetitive DNA
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(trinucleotide; suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)

IT **80146-85-6, Transglutaminase**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)

IT **101985-79-9**, d-CAG
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)

IT **51-85-4**, Cystamine **10121-91-2, Monodansyl cadaverine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

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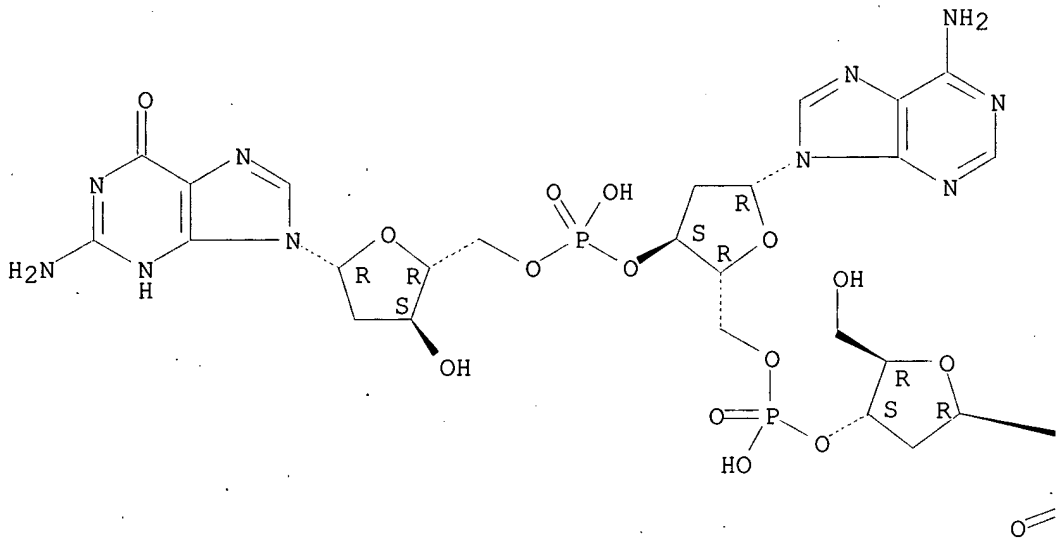
IT **80146-85-6, Transglutaminase**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **101985-79-9**, d-CAG
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)
RN 101985-79-9 HCAPLUS
CN Guanosine, 2'-deoxycytidylyl-(3'.fwdarw.5')-2'-deoxyadenylyl-(3'.fwdarw.5')-2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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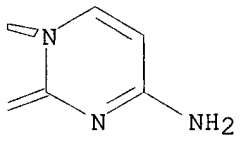

IT **51-85-4**, Cystamine **10121-91-2, Monodansyl cadaverine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with expanded polyglutamine stretch)
RN 51-85-4 HCAPLUS
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-S-S-CH_2-CH_2-NH_2$

RN 10121-91-2 HCAPLUS
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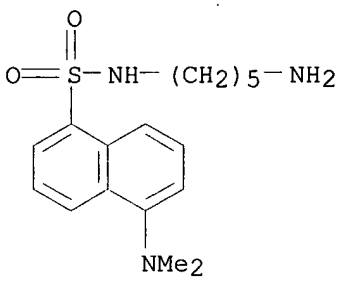


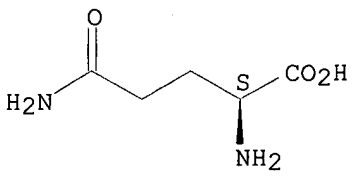
L71 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:768662 HCAPLUS
DN 128:46792
TI **Transglutaminase**-catalyzed inactivation of glyceraldehyde 3-phosphate dehydrogenase and .alpha.-ketoglutarate dehydrogenase complex by polyglutamine domains of pathological length
AU Cooper, Arthur J. L.; Sheu, K. -F. Rex; Burke, James R.; Onodera, Osamu; Strittmatter, Warren J.; Roses, Allen D.; Blass, John P.
CS Department of Biochemistry, Cornell University Medical College, New York, NY, 10021, USA
SO Proceedings of the National Academy of Sciences of the United States of America (**1997**), 94(23), 12604-12609
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
AB Several adult-onset neurodegenerative diseases are caused by genes with expanded CAG triplet repeats within their coding regions and extended polyglutamine (Qn) domains within the expressed proteins. Generally, in clin. affected individuals n .gtoreq. 40. Glyceraldehyde 3-phosphate dehydrogenase binds tightly to four Qn disease proteins, but the significance of this interaction is unknown. The authors now report that purified glyceraldehyde 3-phosphate dehydrogenase is inactivated by tissue **transglutaminase** in the presence of glutathione S-transferase constructs contg. a Qn domain of pathol. length (n = 62 or 81). The dehydrogenase is less strongly inhibited by tissue **transglutaminase** in the presence of constructs contg. shorter Qn domains (n = 0 or 10). Purified .alpha.-ketoglutarate dehydrogenase complex also is inactivated by tissue **transglutaminase** plus glutathione S-transferase constructs contg. pathol.-length Qn domains (n = 62 or 81). Apparently, tissue **transglutaminase**-catalyzed covalent linkages involving the larger poly-Q domains may disrupt cerebral energy metab. in CAG/Qn expansion diseases.
ST GAPDH inhibition polyglutamine tissue **transglutaminase** neurodegeneration
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CAG triplet contg.; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT **Nervous system**
(**Huntington's chorea**; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase,

but do so in the presence of tissue **transglutaminase**)
IT Spinal muscular atrophy
(X-linked spinal and bulbar muscular atrophy; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT Nervous system
(degeneration; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT **Brain, disease**
(**dentatorubral-pallidoluysian** atrophy; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT Metabolism
(energy; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT Disease, animal
(genetic, expansion diseases; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT Protein motifs
(polyglutamine domain; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT **Nervous system**
(**spinocerebellar ataxia**; longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT 9001-50-7, Glyceraldehyde-3-phosphate dehydrogenase **26700-71-0**, Polyglutamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study).
(longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT **80146-85-6**, Tissue **transglutaminase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT **101985-79-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
IT **26700-71-0**, Polyglutamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
RN 26700-71-0 HCAPLUS
CN L-Glutamine, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 56-85-9
CMF C5 H10 N2 O3

Absolute stereochemistry.

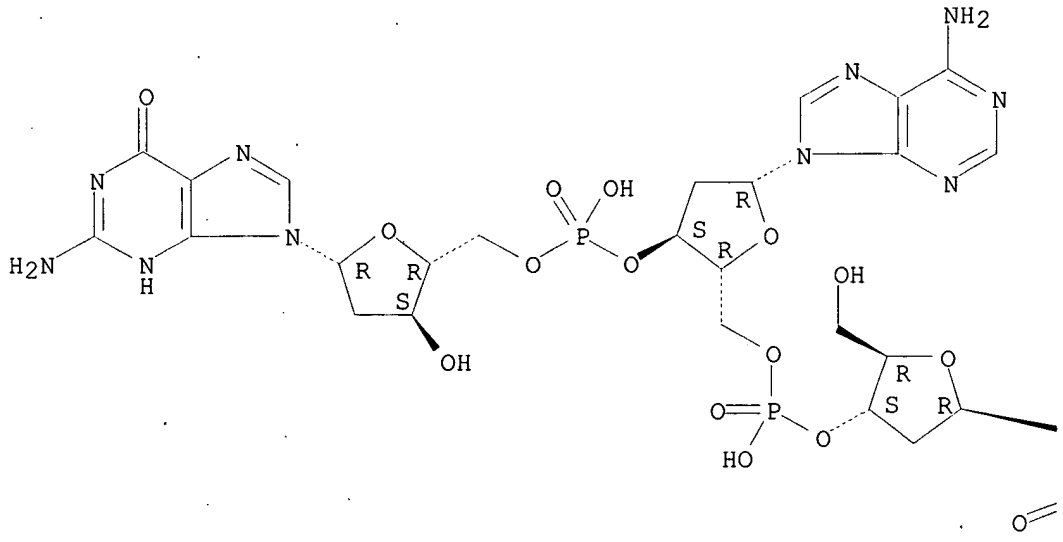


IT **80146-85-6**, Tissue **transglutaminase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **101985-79-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(longer polyglutamine domains by themselves do not inhibit glyceraldehyde 3-phosphate dehydrogenase, but do so in the presence of tissue **transglutaminase**)
RN 101985-79-9 HCAPLUS
CN Guanosine, 2'-deoxycytidylyl-(3'.fwdarw.5')-2'-deoxyadenylyl-(3'.fwdarw.5')-2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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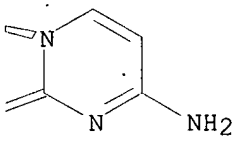


L71 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:409539 HCAPLUS
DN 127:134212
TI Polyglutamine domains are substrates of tissue **transglutaminase**: does **transglutaminase** play a role in expanded CAG/Poly-Q neurodegenerative diseases?
AU Cooper, Arthur J. L.; Sheu, Kwan-Fu Rex; Burke, James R.; Onodera, Osamu; Strittmatter, Warren J.; Roses, Allen D.; Blass, John P.
CS Department of Biochemistry, Cornell University Medical College, New York, NY, USA
SO Journal of Neurochemistry (**1997**), 69(1), 431-434
CODEN: JONRA9; ISSN: 0022-3042
PB Lippincott-Raven
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 7
AB Huntington's disease and six other neurodegenerative diseases are assocd. with abnormal gene products contg. expanded polyglutamine (poly-Q; Qn) domains (n .gtoreq. 40). In the present work, the authors show that glutathione S-transferase (GST) fusion proteins contg. a small, physiol.-length poly-Q domain (GSTQ10) or a large, pathol.-length poly-Q domain (GSTQ62) are excellent substrates of guinea pig liver (tissue) **transglutaminase** and that both GSTQ10 and GSTQ62 are activators of tissue **transglutaminase**-catalyzed hydroxaminolysis of N-.alpha.-carbobenzoxyglutaminylglycine. The present findings have implications for understanding the pathophysiol. mechanisms of expanded CAG/poly-Q domain diseases.
ST **transglutaminase** polyglutamine protein substrate neurodegenerative disease; Huntington **transglutaminase** polyglutamine protein substrate
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(CAG repeat-contg.; proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded

CAG/polyglutamine neurodegenerative diseases)

IT **Nervous system**
(**Huntington's chorea**; proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT Nervous system
(degeneration, trinucleotide repeat; proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(expanded polyglutamine-contg.; proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT Mutation
(expansion, of CAG trinucleotide repeat; proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT Repeat motifs (protein)
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(polyglutamine; proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT Repetitive DNA
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(trinucleotide; proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT **80146-85-6**, Glutaminylpeptide .gamma.-glutamyltransferase
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT **26700-71-0D**, Polyglutamine, proteins contg. **69864-43-3D**, Polyglutamine, proteins contg.
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT **101985-79-9**, d-CAG
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)

IT **80146-85-6**, Glutaminylpeptide .gamma.-glutamyltransferase

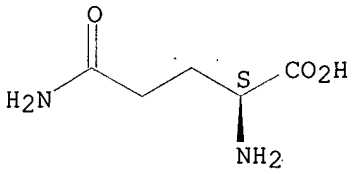
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **26700-71-0D**, Polyglutamine, proteins contg. **69864-43-3D**, Polyglutamine, proteins contg.
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)
RN 26700-71-0 HCAPLUS
CN L-Glutamine, homopolymer (9CI) (CA INDEX NAME)

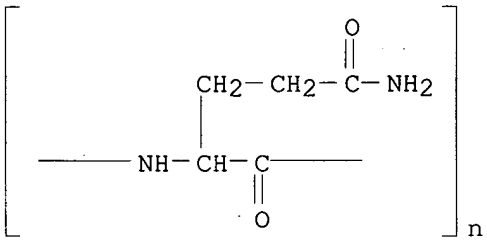
CM 1

CRN 56-85-9
CMF C5 H10 N2 O3

Absolute stereochemistry.



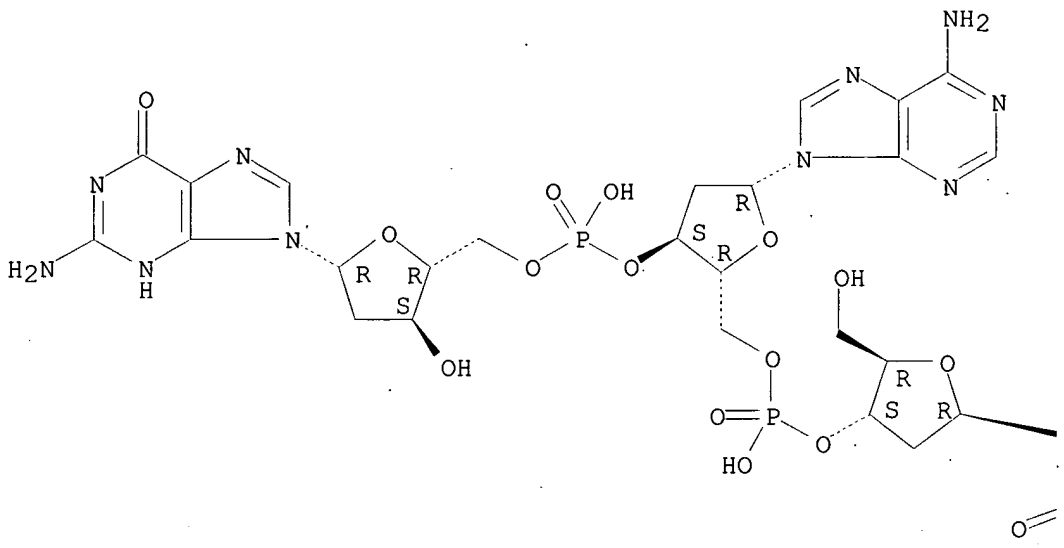
RN 69864-43-3 HCAPLUS
CN Poly[imino[(1S)-1-(3-amino-3-oxopropyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



IT **101985-79-9**, d-CAG
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(proteins contg. polyglutamine domains are substrates of tissue **transglutaminase** and **transglutaminase** may play role in human expanded CAG/polyglutamine neurodegenerative diseases)
RN 101985-79-9 HCAPLUS
CN Guanosine, 2'-deoxycytidylyl-(3'.fwdarw.5')-2'-deoxyadenylyl-(3'.fwdarw.5')-2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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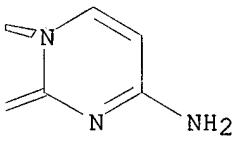


L71 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:746875 HCAPLUS
DN 126:101006
TI Peptides containing glutamine repeats as substrates for **transglutaminase**-catalyzed crosslinking: relevance to diseases of the nervous system
AU Kahlem, P.; Terre, C.; Green, H.; Djian, P.
CS Cent. Natl. Rech. Sci., Cent. Rech. Endocrinol. Mol. Dev., Meudon-Bellevue, 92190, Fr.
SO Proceedings of the National Academy of Sciences of the United States of America (**1996**), 93(25), 14580-14585

CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 7-3 (Enzymes)

AB Many proteins contain reiterated glutamine residues, but polyglutamine of excessive length may result in human disease by conferring new properties on the protein contg. it. One established property of a glutamine residue, depending on the nature of the flanking residues, is its ability to act as an amine acceptor in a **transglutaminase**-catalyzed reaction and to make a glutamyl-lysine cross-link with a neighboring polypeptide. To learn whether glutamine repeats can act as amine acceptors, we have made peptides with variable lengths of polyglutamine flanked by the adjacent amino acid residues in the proteins assocd. with spinocerebellar ataxia type 1 (SCA1), Machado-Joseph disease (SCA3), or dentato-rubral pallidoluysian atrophy (DRPLA) or those residues adjacent to the preferred crosslinking site of involucrin, or solely by arginine residues. The polyglutamine was found to confer excellent substrate properties on any sol. peptide; under optimal conditions, virtually all the glutamine residues acted as amine acceptors in the reaction with glycine ethyl-ester, and lengthening the sequence of polyglutamine increased the reactivity of each glutamine residue. In the presence of **transglutaminase**, peptides contg. polyglutamine formed insol. aggregates with the proteins of brain exts. and these aggregates contained glutamyl-lysine cross-links. Repeated glutamine residues exposed on the surface of a neuronal protein should form cross-linked aggregates in the presence of any **transglutaminase** activated by the presence of Ca2+.

ST **transglutaminase** substrate glutamine calcium

IT **Brain, disease**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**dentatorubral-pallidoluysian** atrophy; peptides contg. glutamine repeats as substrates for **transglutaminase** -catalyzed crosslinking and relevance to nervous system diseases)

IT **Nervous system**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(disease, **spinocerebellar ataxia** 3; peptides contg. glutamine repeats as substrates for **transglutaminase** -catalyzed crosslinking and relevance to nervous system diseases)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(involucrins; peptides contg. glutamine repeats as substrates for **transglutaminase**-catalyzed crosslinking and relevance to nervous system diseases)

IT **Nervous system**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**spinocerebellar ataxia** 1; peptides contg. glutamine repeats as substrates for **transglutaminase** -catalyzed crosslinking and relevance to nervous system diseases)

IT Structure-activity relationship
(**transglutaminase** substrates; peptides contg. glutamine repeats as substrates for **transglutaminase**-catalyzed crosslinking)

IT 7440-70-2, Calcium, biological studies **80146-85-6, Transglutaminase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(peptides contg. glutamine repeats as substrates for **transglutaminase**-catalyzed crosslinking)

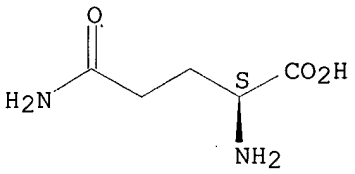
IT 56-85-9, Glutamine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptides contg. glutamine repeats as substrates for **transglutaminase**-catalyzed crosslinking)
IT **26700-71-0**, Polyglutamine **69864-43-3**, Polyglutamine
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(peptides contg. glutamine repeats as substrates for **transglutaminase**-catalyzed crosslinking)
IT **80146-85-6, Transglutaminase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(peptides contg. glutamine repeats as substrates for **transglutaminase**-catalyzed crosslinking)
RN 80146-85-6 HCAPLUS
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **26700-71-0**, Polyglutamine **69864-43-3**, Polyglutamine
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(peptides contg. glutamine repeats as substrates for **transglutaminase**-catalyzed crosslinking)
RN 26700-71-0 HCAPLUS
CN L-Glutamine, homopolymer (9CI) (CA INDEX NAME)

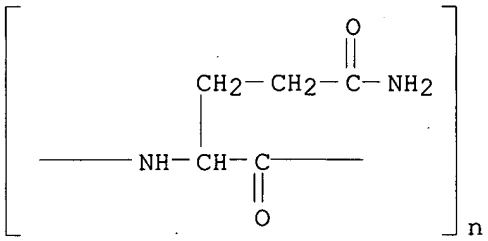
CM 1

CRN 56-85-9
CMF C5 H10 N2 O3

Absolute stereochemistry.



RN 69864-43-3 HCAPLUS
CN Poly[imino[(1S)-1-(3-amino-3-oxopropyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



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STRUCTURE FILE UPDATES:   30 JUN 2003  HIGHEST RN 540462-79-1
DICTIONARY FILE UPDATES:  30 JUN 2003  HIGHEST RN 540462-79-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L72  ANSWER 1 OF 14  REGISTRY  COPYRIGHT 2003 ACS
RN   101985-79-9  REGISTRY
CN   Guanosine, 2'-deoxycytidylyl-(3'.fwdarw.5')-2'-deoxyadenylyl-
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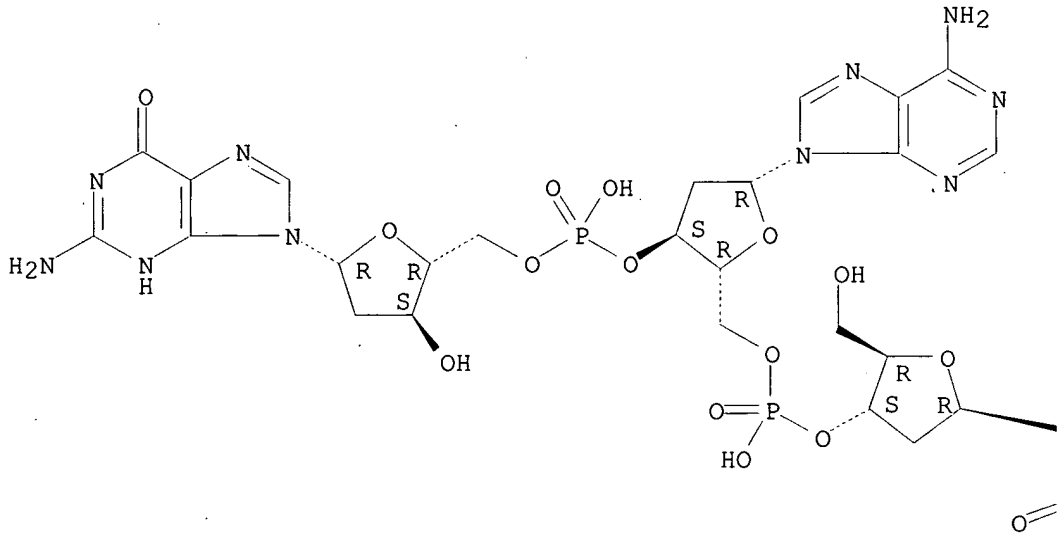
OTHER NAMES:
CN 18: PN: US20030093830 PAGE: 18 claimed sequence
CN 99: PN: WO02072882 TABLE: 3 claimed sequence
CN DCAG
CN Deoxy-CAG trinucleotide
FS STEREOSEARCH
MF C29 H37 N13 O15 P2
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.

PAGE 1-A



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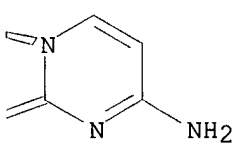

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REFERENCE 7: 138:366424

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REFERENCE 10: 138:301261

L72 ANSWER 2 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **80146-85-6** REGISTRY
CN Glutamyltransferase, glutaminylpeptide .gamma.- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Activa MP
CN Activa Supercurd
CN Activa TG
CN Activa TG-K
CN Activa TG-M
CN Activa TG-S
CN Activa TG-TI
CN Activa WM
CN Akuthiba TG-S
CN E.C. 2.3.2.13
CN Glutaminylpeptide .gamma.-glutamyltransferase
CN Koshikeep
CN Polyamine transglutaminase
CN PPQ 6117
CN Tissue transglutaminase
CN Transglutaminase
DR 300711-04-0
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CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, EMBASE, MSDS-OHS, PIRA, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

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REFERENCE 7: 138:400779

REFERENCE 8: 138:400693

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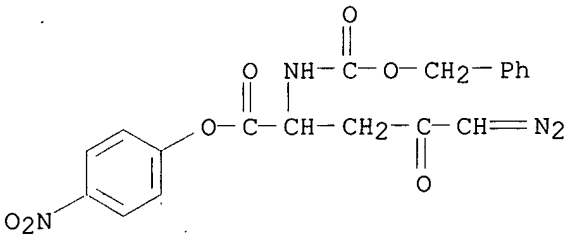
REFERENCE 10: 138:399774

L72 ANSWER 3 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **74389-76-7** REGISTRY
CN Norvaline, 5-diazo-4-oxo-N-[(phenylmethoxy)carbonyl]-, 4-nitrophenyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C19 H16 N4 O7
LC STN Files: CA, CAPLUS, TOXCENTER



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REFERENCE 4: 93:68458

L72 ANSWER 4 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **69864-43-3** REGISTRY
CN Poly[imino[(1S)-1-(3-amino-3-oxopropyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Poly[imino[1-(3-amino-3-oxopropyl)-2-oxo-1,2-ethanediyl]], (S)-
OTHER NAMES:
CN Poly(glutamine), SRU
CN Poly(L-glutamine), SRU
CN Poly-L-glutamine
CN Polyglutamine
DR 26603-78-1
MF (C5 H8 N2 O2)n
CI PMS, COM

PCT Polyamide
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, EMBASE, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL

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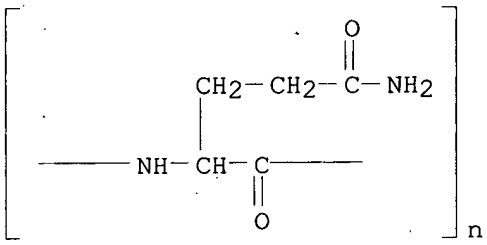

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REFERENCE 5: 138:390990

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REFERENCE 7: 138:335249

REFERENCE 8: 138:318968

REFERENCE 9: 138:314634

REFERENCE 10: 138:202962

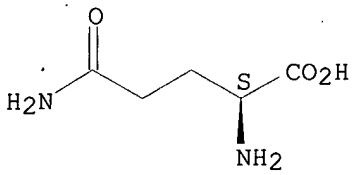
L72 ANSWER 5 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **26700-71-0** REGISTRY
CN L-Glutamine, homopolymer (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamine, L-, peptides (8CI)
OTHER NAMES:
CN Glutamine homopolymer
CN Poly-L-glutamine
CN Polyglutamine
FS STEREOSEARCH
MF (C5 H10 N2 O3)x
CI PMS, COM
PCT Polyamide, Polyamide formed
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CEN, CIN, EMBASE, MEDLINE, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL

RELATED POLYMERS AVAILABLE WITH POLYLINK

CM 1

CRN 56-85-9
CMF C5 H10 N2 O3

Absolute stereochemistry.



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REFERENCE 8: 138:382993

REFERENCE 9: 138:382992

REFERENCE 10: 138:380166

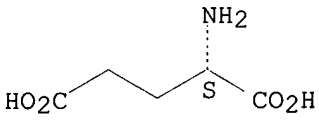
L72 ANSWER 6 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **25513-46-6** REGISTRY
CN L-Glutamic acid, homopolymer (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, L-, peptides (8CI)
OTHER NAMES:
CN .alpha.-L-Glutamic acid polymer
CN .gamma.-L-Polyglutamic acid
CN Glutamic acid homopolymer
CN Glutamic acid polymer
CN L-Glutamic acid polymer
CN PGA
CN Poly(.alpha.-L-glutamic acid)
CN Poly(L-glutamic acid)
CN Poly-L-glutamate
CN Polyglutamic acid
FS STEREOSEARCH
DR 24938-00-9, 115529-71-0, 66415-63-2, 141982-72-1, 84960-48-5, 26717-13-5
MF (C5 H9 N O4)x
CI PMS, COM
PCT Polyamide, Polyamide formed
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2, USPATFULL
(*File contains numerically searchable property data)

RELATED POLYMERS AVAILABLE WITH POLYLINK

CM 1

CRN 56-86-0
CMF C5 H9 N O4

Absolute stereochemistry.



1890 REFERENCES IN FILE CA (1957 TO DATE)
391 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1896 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 139:16809

REFERENCE 2: 139:5708

REFERENCE 3: 139:3049

REFERENCE 4: 139:979

REFERENCE 5: 138:411206

REFERENCE 6: 138:406739

REFERENCE 7: 138:398299

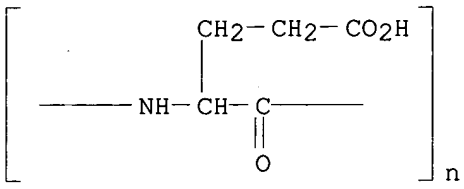
REFERENCE 8: 138:397896

REFERENCE 9: 138:390607

REFERENCE 10: 138:373954

L72 ANSWER 7 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **24991-23-9** REGISTRY
CN Poly[imino[(1S)-1-(2-carboxyethyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Poly[iminocarbonyl(3-carboxypropylidene)], L- (8CI)
CN Poly[imino[1-(2-carboxyethyl)-2-oxo-1,2-ethanediyl]], (S)-
OTHER NAMES:
CN Glutamic acid homopolymer, SRU
CN L-Glutamic acid homopolymer, SRU
CN Poly(.alpha.-glutamic acid), SRU
CN Poly(.alpha.-L-glutamic acid), SRU
CN Poly(L-.alpha.-glutamyl)
CN Poly(L-glutamic acid), SRU
CN Poly(L-glutamyl)
CN Poly-L-glutamate SRU
CN Polyglutamic acid, SRU
DR 124224-52-8, 37453-50-2, 78678-46-3, 26063-12-7, 26915-14-0
MF (C5 H7 N O3)n
CI PMS, COM
PCT Polyamide
LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, EMBASE, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPAT2, USPATFULL

RELATED POLYMERS AVAILABLE WITH POLYLINK



1430 REFERENCES IN FILE CA (1957 TO DATE)
320 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1435 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 139:5708

REFERENCE 2: 139:979

REFERENCE 3: 138:406739

REFERENCE 4: 138:398299

REFERENCE 5: 138:397896

REFERENCE 6: 138:390607

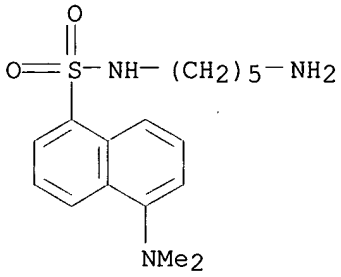
REFERENCE 7: 138:373954

REFERENCE 8: 138:369333

REFERENCE 9: 138:369188

REFERENCE 10: 138:354701

L72 ANSWER 8 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **10121-91-2** REGISTRY
CN 1-Naphthalenesulfonamide, N-(5-aminopentyl)-5-(dimethylamino)- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Dansylcadaverine
CN Monodansylcadaverine
CN N-(5-Aminopentyl)-5-dimethylamino-1-naphthalenesulfonamide
FS 3D CONCORD
DR 99473-69-5
MF C17 H25 N3 O2 S
LC STN Files: ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, NIOSHTIC, TOXCENTER, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

263 REFERENCES IN FILE CA (1957 TO DATE)
12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
263 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:272300

REFERENCE 2: 138:233597

REFERENCE 3: 138:122793

REFERENCE 4: 137:245263

REFERENCE 5: 137:105614

REFERENCE 6: 136:337048

REFERENCE 7: 136:66576

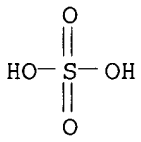
REFERENCE 8: 136:1616

REFERENCE 9: 135:343279

REFERENCE 10: 135:177036

L72 ANSWER 9 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **7758-98-7** REGISTRY
CN Sulfuric acid copper(2+) salt (1:1) (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Blue Copper
CN Blue stone
CN Blue vitriol
CN Copper monosulfate
CN Copper sulfate
CN Copper sulfate (1:1)
CN Copper sulfate (CuSO4)
CN Copper(2+) sulfate
CN Copper(2+) sulfate (1:1)
CN Copper(II) sulfate
CN Cuivrol
CN Cupric sulfate
CN Cupric sulfate anhydrous
CN Cupric sulphate
CN Delcup
CN Hylinec
CN Incracide 10A
CN Incracide E 51
CN MAC 570

CN Monocopper sulfate
CN Roman vitriol
CN Sulfuric acid, copper(2+) salt (1:1)
DR 139939-69-8
MF Cu . H2 O4 S
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (7664-93-9)



Cu(II)

17916 REFERENCES IN FILE CA (1957 TO DATE)
229 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
17932 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 139:16836

REFERENCE 2: 139:16113

REFERENCE 3: 139:15101

REFERENCE 4: 139:14719

REFERENCE 5: 139:13883

REFERENCE 6: 139:11485

REFERENCE 7: 139:7579

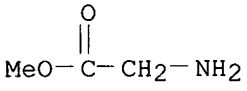
REFERENCE 8: 139:6038

REFERENCE 9: 139:5709

REFERENCE 10: 139:2372

L72 ANSWER 10 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **616-34-2** REGISTRY
CN Glycine, methyl ester (6CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (Methoxycarbonyl)methylamine
CN Glycine O-methyl ester
CN Methyl aminoacetate
CN Methyl glycinate
CN Methyl glycine

FS 3D CONCORD
MF C3 H7 N O2
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1002 REFERENCES IN FILE CA (1957 TO DATE)
44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1005 REFERENCES IN FILE CAPLUS (1957 TO DATE)
27 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:7371

REFERENCE 2: 139:6418

REFERENCE 3: 138:385730

REFERENCE 4: 138:385680

REFERENCE 5: 138:385420

REFERENCE 6: 138:353826

REFERENCE 7: 138:353778

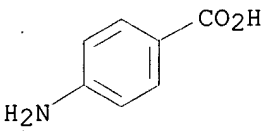
REFERENCE 8: 138:303687

REFERENCE 9: 138:287984

REFERENCE 10: 138:260997

L72 ANSWER 11 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **150-13-0** REGISTRY
CN Benzoic acid, 4-amino- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzoic acid, p-amino- (8CI)
OTHER NAMES:
CN 4-Aminobenzoic acid
CN 4-Carboxyaniline
CN Amben
CN Aniline-4-carboxylic acid
CN Anti-Chromotrichia factor
CN Anticanitic vitamin
CN Anticantic vitamin
CN Antichromotrichia factor
CN Bacterial vitamin H1
CN Chromotrichia factor
CN Hachemina
CN p-Aminobenzoic acid
CN p-Carboxyaniline

CN p-Carboxyphenylamine
CN PAB
CN PABA
CN Pabacyd
CN Pabafilm
CN Pabamine
CN Paraminol
CN Paranate
CN Romavit
CN Sunbrella
CN Trichochromogenic factor
CN Vitamin BX
CN Vitamin H'
FS 3D CONCORD
DR 8014-65-1
MF C7 H7 N O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7888 REFERENCES IN FILE CA (1957 TO DATE)
503 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7905 REFERENCES IN FILE CAPLUS (1957 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:12012

REFERENCE 2: 139:6868

REFERENCE 3: 139:6791

REFERENCE 4: 139:6446

REFERENCE 5: 139:3078

REFERENCE 6: 138:411210

REFERENCE 7: 138:409366

REFERENCE 8: 138:406796

REFERENCE 9: 138:401298

REFERENCE 10: 138:398399

L72 ANSWER 12 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **110-60-1** REGISTRY
CN 1,4-Butanediamine (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Tetramethylenediamine (7CI)
OTHER NAMES:
CN .alpha.,.omega.-Butanediamine
CN 1,4-Butylenediamine
CN 1,4-Diamino-n-butane
CN 1,4-Diaminobutane
CN 1,4-Tetramethylenediamine
CN Putrescin
CN Putrescine
FS 3D CONCORD
MF C4 H12 N2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

$H_2N-(CH_2)_4-NH_2$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10660 REFERENCES IN FILE CA (1957 TO DATE)
425 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10670 REFERENCES IN FILE CAPLUS (1957 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:7684

REFERENCE 2: 139:5929

REFERENCE 3: 139:3614

REFERENCE 4: 139:3528

REFERENCE 5: 139:2339

REFERENCE 6: 139:2338

REFERENCE 7: 138:411107

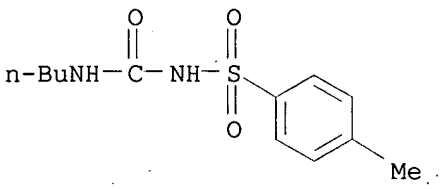
REFERENCE 8: 138:411018

REFERENCE 9: 138:406735

REFERENCE 10: 138:406609

L72 ANSWER 13 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **64-77-7** REGISTRY
CN Benzenesulfonamide, N-[(butylamino)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN Urea, 1-butyl-3-(p-tolylsulfonyl)- (8CI)
OTHER NAMES:
CN 1-Butyl-3-(p-methylphenylsulfonyl)urea
CN 1-Butyl-3-(p-tolylsulfonyl)urea
CN 3-(p-Tolyl-4-sulfonyl)-1-butylurea
CN Aglicid
CN Arkozal
CN Artosin
CN Artozin
CN Butamid
CN Butamide
CN D 860
CN Diaben
CN Diabetamid
CN Diabetol
CN Diabuton
CN Diasulfon
CN Dolipol
CN Glyconon
CN HLS 831
CN Ipoglicone
CN Mobenol
CN N-(4-Methylbenzenesulfonyl)-N'-butylurea
CN N-(4-Methylphenylsulfonyl)-N'-butylurea
CN N-(p-Methylbenzenesulfonyl)-N'-butylurea
CN N-(p-Tolylsulfonyl)-N'-butylcarbamide
CN N-(Sulfonyl-p-methylbenzene)-N'-n-butylurea
CN N-Butyl-N'-(4-methylphenylsulfonyl)urea
CN N-Butyl-N'-(p-tolylsulfonyl)urea
CN N-Butyl-N'-p-toluenesulfonylurea
CN N-n-Butyl-N'-tosylurea
CN Orabet
CN Oralin
CN Orezan
CN Orinase
CN Orinaz
CN Oterben
CN Pramidex
CN Rastinon
CN Tolbusal
CN Tolbutamid
CN Tolbutamide
CN Toluina
CN Tolumid
CN Tolumide
CN Toluvan
CN U 2043
CN Willbutamide
FS 3D CONCORD
DR 100735-34-0
MF C12 H18 N2 O3 S
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3574 REFERENCES IN FILE CA (1957 TO DATE)
25 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3577 REFERENCES IN FILE CAPLUS (1957 TO DATE)
74 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:294

REFERENCE 2: 138:396425

REFERENCE 3: 138:395332

REFERENCE 4: 138:378974

REFERENCE 5: 138:378518

REFERENCE 6: 138:378502

REFERENCE 7: 138:378464

REFERENCE 8: 138:378406

REFERENCE 9: 138:374137

REFERENCE 10: 138:368761

L72 ANSWER 14 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN **51-85-4** REGISTRY
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethylamine, 2,2'-dithiobis- (8CI)
OTHER NAMES:
CN .beta.,.beta.'-Diaminodiethyl disulfide
CN .beta.-Mercaptoethylamine disulfide
CN 1,6-Diamino-3,4-dithiahexane
CN 2,2'-Dithiobis[ethanamine]
CN 2,2'-Dithiobis[ethylamine]
CN 2,2'-Dithiodiethylamine
CN 2-Aminoethane disulfide
CN 2-Aminoethyl disulfide
CN Bis(.beta.-aminoethyl) disulfide
CN Bis(2-aminoethyl) disulfide
CN Cystamine
CN Cysteinamine disulfide
CN Cystineamine
CN Decarboxycystine
CN L 1591
CN Mercamine disulfide
CN Merkamine disulfide
FS 3D CONCORD
MF C4 H12 N2 S2
CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

$H_2N-CH_2-CH_2-S-S-CH_2-CH_2-NH_2$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1699 REFERENCES IN FILE CA (1957 TO DATE)
62 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1702 REFERENCES IN FILE CAPLUS (1957 TO DATE)
25 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:13807

REFERENCE 2: 138:395986

REFERENCE 3: 138:384238

REFERENCE 4: 138:338123

REFERENCE 5: 138:268299

REFERENCE 6: 138:216948

REFERENCE 7: 138:203675

REFERENCE 8: 138:188004

REFERENCE 9: 138:175678

REFERENCE 10: 138:140904

=> fil biosis
FILE 'BIOSIS' ENTERED AT 16:14:00 ON 01 JUL 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 25 June 2003 (20030625/ED)

=> d all tot l82

L82 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:120800 BIOSIS
DN PREV199800120800
TI Suppression of aggregate formation and apoptosis by **transglutaminase** inhibitors in cells expressing truncated DRPLA protein with an expanded polyglutamine stretch.
AU Igarashi, Shuichi; Koide, Reiji (1); Shimohata, Takayoshi; Yamada, Mitsunori; Hayashi, Yasuko; Takano, Hiroki; Date, Hidetoshi; Oyake,

Mutsuo; Sato, Toshiya; Sato, Aki; Egawa, Shigekimi; Ikeuchi, Takeshi; Tanaka, Hajime; Nakano, Ryoichi; Tanaka, Keiko; Hozumi, Isao; Inuzuka, Takashi; Takahashi, Hitoshi; Tsuji, Shoji
CS (1) Dep. Neurol., Niigatta Univ., 1-757 Asahimachi Niigata 951 Japan
SO Nature Genetics, (**Feb.**, **1998**) Vol. 18, No. 2, pp. 111-117.
ISSN: 1061-4036.
DT Article
LA English
AB To elucidate the molecular mechanisms whereby expanded polyglutamine stretches elicit a gain of toxic function, we expressed full-length and truncated DRPLA (**dentatorubral-pallidoluysian atrophy**) cDNAs with or without expanded **CAG** repeats in COS-7 cells. We found that truncated DRPLA proteins containing an expanded polyglutamine stretch form filamentous peri- and intranuclear aggregates and undergo apoptosis. The apoptotic cell death was partially suppressed by the **transglutaminase** inhibitors cystamine and **monodansyl cadaverine** (but not putrescine), suggesting involvement of a **transglutaminase** reaction and providing a potential basis for the development of therapeutic measures for **CAG**-repeat expansion diseases.
CC Genetics and Cytogenetics - Animal *03506
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Enzymes - Chemical and Physical *10806
Pathology, General and Miscellaneous - General *12502
Pathology, General and Miscellaneous - Necrosis *12510
BC Cercopithecidae 86205
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics)
IT Diseases
CAG-repeat expansion diseases: genetic disease
IT Chemicals & Biochemicals
cDNA [complementary DNA]; **transglutaminase**; DRPLA protein [**dentatorubral-pallidoluysian atrophy** protein]: expanded polyglutamine stretch, toxic function
IT Miscellaneous Descriptors
aggregate formation; apoptotic cell death
ORGN Super Taxa
Cercopithecidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
COS-7 (Cercopithecidae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Primates; Nonhuman Vertebrates; Primates; Vertebrates
RN **80146-85-6** (**TRANSGLUTAMINASE**)
26700-71-0Q (POLYGLUTAMINE)
69864-43-3Q (POLYGLUTAMINE)

L82 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:300704 BIOSIS
DN PREV199799599907
TI Pharmacologic inhibition of **transglutaminase**-induced cross-linking of Alzheimer's amyloid beta-peptide.
AU Zhang, Wei; Johnson, Brett R.; Bjornsson, Thorir D. (1)
CS (1) Div. Clin. Pharmacol., Dep. Med., Jefferson Med. Coll., 1100 Walnut St., MOB-601, Philadelphia, PA 19107 USA
SO Life Sciences, (1997) Vol. 60, No. 25, pp. 2323-2332.
ISSN: 0024-3205.
DT Article
LA English
AB The brain of Alzheimer's disease (AD) patients contains deposits of amyloid beta-peptide (A-beta). Recent studies have shown that A-beta is a substrate for tissue **transglutaminase** (TGase), which induces the

formation of cross-linked dimers and polymers, and that tacrine, indomethacin and deferoxamine, which have widely different chemical structures, attenuate the progression of symptoms of AD. This report evaluated the potential of a total of ten different pharmacological agents to inhibit TGase-induced cross-linking of A-beta, including known TGase inhibitors (**dansylcadaverine**, spermine), non-steroidal anti-inflammatory drugs (indomethacin, meclofenamic acid, diflunisal, salicylic acid), monoamine oxidase inhibitors (tranylcypromine, phenelzine), an acetylcholinesterase inhibitor (tacrine), and an iron chelating agent (deferoxamine). All but one (salicylic acid) of these ten agents had an inhibitory effect on TGase-induced A-beta cross-linking. These results suggest that inhibition of TGase-induced cross-linking of A-beta is a potential pharmacologic target for the treatment of AD. A method is also presented for the determination of percent inhibition of TGase-induced A-beta cross-linking based on the separated monomer, dimer and polymer bands on SDS-PAGE gels.

CC Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Chemical and Physical *10806
Pharmacology - Neuropharmacology *22024

IT Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics); Pharmacology

IT Chemicals & Biochemicals
TRANSGLUTAMINASE; AMYLOID; **DANSYLCADAVERINE**; SPERMINE; INDOMETHACIN; MECLOFENAMIC ACID; DIFLUNISAL; SALICYLIC ACID; TRANYLCYPROMINE; PHENELZINE; TACRINE; DEFEROXAMINE; EC 2.3.2.13

IT Miscellaneous Descriptors
ALZHEIMER'S DISEASE; AMYLOID BETA-PEPTIDE; ANTI-ALZHEIMER'S AGENT; ANTIINFLAMMATORY-DRUG; BIOCHEMISTRY AND BIOPHYSICS; **DANSYLCADAVERINE**; DEFEROXAMINE; DIFLUNISAL; EC 2.3.2.13; INDOMETHACIN; MECLOFENAMIC ACID; NERVOUS SYSTEM DISEASE; PHARMACOLOGY; PHENELZINE; SALICYLIC ACID; SPERMINE; TACRINE; **TRANSGLUTAMINASE** ; **TRANSGLUTAMINASE** INHIBITOR; **TRANSGLUTAMINASE** -INDUCED CROSS-LINKING INHIBITION; TRANYLCYPROMINE

RN **80146-85-6** (**TRANSGLUTAMINASE**)
11061-24-8 (AMYLOID)
10121-91-2 (**DANSYLCADAVERINE**)
71-44-3 (SPERMINE)
53-86-1 (INDOMETHACIN)
644-62-2 (MECLOFENAMIC ACID)
22494-42-4 (DIFLUNISAL)
69-72-7 (SALICYLIC ACID)
155-09-9 (TRANYLCYPROMINE)
51-71-8 (PHENELZINE)
321-64-2 (TACRINE)
70-51-9 (DEFEROXAMINE)
80146-85-6 (EC 2.3.2.13)

L82 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:113658 BIOSIS
DN PREV199799412861
TI Microtubules and microfilaments participate in the inhibition of synaptosomal noradrenaline release by tetanus toxin.
AU Ashton, Anthony C.; Dolly, J. Oliver (1)
CS (1) Dep. Biochemistry, Imperial Coll., London SW7 2AY UK
SO Journal of Neurochemistry, (1997) Vol. 68, No. 2, pp. 649-658.
ISSN: 0022-3042.
ticle
h
is toxin (TeTX) has been demonstrated to inhibit transmitter release
o mechanisms: Zn-2+dependent proteolytic cleavage of synaptobrevin

and activation of a neuronal **transglutaminase**. Herein, attenuation of TeTX-induced blockade of noradrenaline release from synaptosomes was achieved by prior disassembly of microfilaments with cytochalasin D or breakdown of microtubules by colchicine or nocodazole. These drugs and **monodansylcadaverine**, a **transglutaminase** inhibitor, displayed some additivity in antagonizing the inhibitory effect of the toxin on synaptosomal transmitter release; as none of them reduced synaptobrevin cleavage, all appear to work independently of the toxin's proteolytic action. Prior stabilization of microtubules with taxol prevented the antagonism seen with colchicine, highlighting that this cytoskeletal component is the locus of the effect of colchicine. Replacement of Ca-2+ with Ba-2+ caused disappearance of the fraction of evoked secretion whose inhibition by TeTX is reliant on polymerized actin but did not alter the blockade by toxin that is dependent on microtubules. Two temporally distinguished phases of release were reduced by TeTX, and colchicine lessened its effects on both. Blockade of the fast phase (ltoreq 10 s) of secretion by TeTX was unaffected by cytochalasin D, but it clearly antagonized the toxin-induced inhibition of the slow (10-s to gtoreq 5-min) component; it is notable that such antagonism was accentuated during a second bout of evoked release. These findings are consistent with sustained release requiring dissociation of synaptic vesicles from the microfilaments, a step that seems to be perturbed by TeTX.

CC Cytology and Cytochemistry - Animal *02506
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Endocrine System - Neuroendocrinology *17020
Nervous System - Pathology *20506
Toxicology - General; Methods and Experimental *22501
Physiology and Biochemistry of Bacteria *31000

BC Muridae *86375

IT Major Concepts
Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Nervous System (Neural Coordination); Physiology; Toxicology

IT Chemicals & Biochemicals
NORADRENALINE; NOREPINEPHRINE; **TRANSGLUTAMINASE**

IT Miscellaneous Descriptors
MICROFILAMENT; MICROTUBULE; NERVOUS SYSTEM; NOREPINEPHRINE; SYNAPTIC VESICLE; SYNAPTOBREVIN; SYNAPTOSOMAL RELEASE; TETANUS TOXIN; **TRANSGLUTAMINASE**

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rat (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

RN 51-41-2 (NORADRENALINE)
51-41-2 (NOREPINEPHRINE)
80146-85-6 (TRANSGLUTAMINASE)

L82 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1996:416490 BIOSIS
DN PREV199699138846
TI Role of **transglutaminase** in (3H)5-HT release from synaptosomes and in the inhibitory effect of tetanus toxin.
AU Gobbi, M. (1); Frittoli, E.; Mennini, T.
CS (1) Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, 20157 Milano Italy
SO Neurochemistry International, (1996) Vol. 29, No. 2, pp. 129-134. ISSN: 0197-0186.
DT Article

LA English
AB It has been suggested that the Ca-2+-dependent enzyme **transglutaminase** (TGase) may suppress vesicular neurotransmitter release and mediate the inhibitory effect of tetanus toxin (TetTx) on exocytosis. The aim of the present study was to test this in a model of (3H)5-HT release from superfused rat cortical synaptosomes. **Monodansylcadaverine**, a synthetic amine chat acts as an alternative substrate for TGase, showed dose-dependent releasing activity which, however, was Ca-2+-independent, being maintained in a Ca-2+-free buffer (containing EGTA) or using synaptosomes preloaded with the intracellular Ca-2+ chelator BAPTA. Preincubation of synaptosomes with RS-48373, an irreversible TGase inactivator, resulted in marked (64%) and persistent inhibition of endogenous TGase but did not alter basal and K+-induced (3H)5-HT release. Preincubation of synaptosomes with 10 nM TetTx resulted in 52% inhibition of K+-induced (3H)5-HT release, and this effect was not antagonized in RS-48373-treated synaptosomes. The inhibitory effect of TetTx was significantly antagonized by 20 mM captopril, a metalloendoprotease inhibitor, confirming in rat brain synaptosomes that TetTx inhibits exocytosis by acting as a metalloendoprotease. These results suggest that TGase is not involved in controlling (3H)5-HT release from resting and depolarized synaptosomes, or in the inhibitory effect of TetTx.
CC Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Minerals 10069
Enzymes - Physiological Studies *10808
Endocrine System - Neuroendocrinology *17020
Muscle - Pathology *17506
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Toxicology - General; Methods and Experimental *22501
BC Muridae *86375
IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Muscular System (Movement and Support); Nervous System (Neural Coordination); Toxicology
IT Chemicals & Biochemicals
TRANSGLUTAMINASE; CALCIUM (II); POTASSIUM (I); SEROTONIN
IT Miscellaneous Descriptors
CALCIUM (II); CORTEX; POTASSIUM (I); SEROTONIN
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **80146-85-6** (**TRANSGLUTAMINASE**)
14127-61-8 (CALCIUM (II))
24203-36-9 (POTASSIUM (I))
50-67-9 (SEROTONIN)

L82 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1987:29797 BIOSIS
DN BA83:19731
TI CYTOTOXIC EFFECTS OF **MONODANSYLCADAVERINE** AND METHYLAMINE IN PRIMARY CULTURES OF RAT CEREBELLAR NEURONS.
AU GILAD G M; GILAD V H
CS VA MED. CENT., SPINAL CORD INJURY RES., 1400 VETERANS OF FOREIGN WARS PARKWAY, BOSTON, MASS. 02132, USA.
SO INT J DEV NEUROSCI, (1986) 4 (5), 401-406.
CODEN: IJDND6. ISSN: 0736-5748.
FS BA; OLD
LA English

AB The effects of **dansylcadaverine** and methylamine, competitive inhibitors of **transglutaminase**, were examined in primary cultures of dissociated rat cerebellar neurons. Addition of the drugs at plating time resulted 24 hr later in irreversible cytotoxic effects evidenced by failure of aggregation and neurite formation. Cytotoxicity was dose-dependent with methylamine being more potent (IC50 = 20 .mu.M) than **dansylcadaverine** (IC50 = 30 .mu.M). The cytotoxic effects were less potent when drugs were added 24 hr after plating, the time when neurons had already begun to extend neurites. Drugs were effective in the various sera and heat-inactivated sera tested. We concluded that low doses of methylamine and **dansylcadaverine** have potent toxic effects on primary neuronal cultures.

CC Cytology and Cytochemistry - Animal *02506
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Comparative *12503
Pathology, General and Miscellaneous - Necrosis 12510
Nervous System - Pathology *20506
Toxicology - Pharmacological Toxicology *22504
Tissue Culture, Apparatus, Methods and Media 32500
In Vitro Studies, Cellular and Subcellular 32600
Plant Physiology, Biochemistry and Biophysics - Chemical Constituents 51522
Pharmacognosy and Pharmaceutical Botany 54000

BC Bovidae 85715
Hominidae 86215
Muridae 86375

IT Miscellaneous Descriptors
FETAL CALF HUMAN **TRANSGLUTAMINASE** INHIBITORS

RN 74-89-5 (METHYLAMINE)
10121-91-2 (**MONODANSYLCADAVERINE**)
80146-85-6 (**TRANSGLUTAMINASE**)

L82 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1983:209038 BIOSIS
DN BA75:59038
TI BRAIN **TRANS GLUTAMINASE** EC-2.3.2.13 IN-VITRO CROSS LINKING OF HUMAN NEURO FILAMENT PROTEINS INTO INSOLUBLE POLYMERS.
AU SELKOE D J; ABRAHAM C; IHARA Y
CS RALPH LOWELL LABORATOIRES, MAILMAN RESEARCH CENT., MCLEAN HOSP., BELMONT, MASS. 02178.
SO PROC NATL ACAD SCI U S A, (1982) 79 (19), 6070-6074.
CODEN: PNASA6. ISSN: 0027-8424.
FS BA; OLD
LA English

AB The accumulation in aged human neurons of insoluble, high-MW filamentous polymers apparently linked by nondisulfide covalent bonds led to the examination of human brain for the presence of **transglutaminase** (EC 2.3.2.13) and endogenous protein substrates for this crosslinking enzyme. The presence of a transamidating enzyme that can covalently crosslink brain proteins into insoluble polymers in vitro by forming .gamma.-glutamyl-.epsilon.-lysine intermolecular bridges was demonstrated. Brain **transglutaminase** is Ca2+ dependent, has an electrophoretic mobility similar to that of erythrocyte **transglutaminase** and is active in human postmortem brain from aged normal individuals and patients with Alzheimer disease (senile dementia). Brain neurofilament fractions incubated in the presence of **transglutaminase**, Ca2+ and the fluorescent amine **dansylcadaverine** form a fluorescent, nondisulfide-bonded insoluble polymer; this process is associated with a decrease in the amount of soluble neurofilament polypeptides in the preparation. EM of the polymeric material reveals an extensive network of connecting filaments, which can be immunostained with various neurofilament antisera. Cystamine, an inhibitor of **transglutaminase**, prevents the neurofilament crosslinking. Glial

filaments and myelin basic protein can also serve as substrates of brain **transglutaminase** in vitro. Although Alzheimer disease-type paired helical filaments were not formed under the specific in vitro coinditions employed, the data suggest 1 possible mechanism for the covalent crosslinking of filaments into insoluble polymers during human neuronal aging.

CC Microscopy Techniques - Electron Microscopy 01058
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066
Biochemical Studies - Minerals 10069
Biophysics - Molecular Properties and Macromolecules 10506
Enzymes - Physiological Studies *10808
Anatomy and Histology, General and Comparative - Microscopic and Ultramicroscopic Anatomy *11108
Metabolism - Proteins, Peptides and Amino Acids *13012
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Gerontology *24500
Developmental Biology - Embryology - Morphogenesis, General *25508

BC Hominidae 86215

IT Miscellaneous Descriptors
ELECTRON MICROSCOPY CYSTAMINE **DANSYL CADAVERINE**
ALZHEIMER DISEASE AGING MYELIN BASIC PROTEIN NEURONAL AGING CALCIUM

RN 51-85-4 (CYSTAMINE)
7440-70-2 (CALCIUM)
10121-91-2 (**DANSYL CADAVERINE**)
80146-85-6 (EC-2.3.2.13)
80146-85-6 (**TRANS GLUTAMINASE**)

L82 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1983:79120 BIOSIS
DN BR25:4120
TI REGULATION OF ORNITHINE DECARBOXYLASE EC-4.1.1.17 ACTIVITY IN CULTURED GLIOMA CELLS BY **TRANS GLUTAMINASE** EC-2.3.2.13.
AU KORNER G; BACHRACH U
CS DEP. MOL. BIOL., HEBREW UNIV.-HADASSAH MED. SCH., JERUSALEM.
SO THE 1982 ANNUAL MEETING OF THE ISRAEL BIOCHEMICAL SOCIETY IN CONJUNCTION WITH THE SECTION FOR BIOTECHNOLOGY AND THE ISRAEL BIOPHYSICAL SOCIETY, REHOVOT, ISRAEL, APRIL 11-12, 1982. ISR J MED SCI. (1982) 18 (6), 11. CODEN: IJMDAI. ISSN: 0021-2180.
DT Conference
FS BR; OLD
LA English

CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal 02506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Chemical and Physical 10806
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies 15002
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology 20506
Neoplasms and Neoplastic Agents - Neoplastic Cell Lines 24005
Developmental Biology - Embryology - Morphogenesis, General *25508
Tissue Culture, Apparatus, Methods and Media 32500

BC Bovidae 85715
Muridae 86375

IT Miscellaneous Descriptors
ABSTRACT RAT C-6 BU-1 CELLS PUTRESCINE ISOPROTERENOL FETAL CALF SERUM **DANSYL CADAVERINE** GROWTH DIFFERENTIATION

RN 110-60-1 (PUTRESCINE)
7683-59-2 (ISOPROTERENOL)
9024-60-6 (ORNITHINE DECARBOXYLASE EC-4.1.1.17)
10121-91-2 (**DANSYL CADAVERINE**)
80146-85-6 (EC-2.3.2.13)
80146-85-6 (**TRANS GLUTAMINASE**)

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FILE LAST UPDATED: 30 JUN 2003 <20030630/UP>
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GUIDES, PLEASE VISIT:
http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d l91 all abeq tech abex tot

L91 ANSWER 1 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN 2000-147134 [13] WPIX
DNC C2000-046006
TI Treatment of neurodegenerative diseases and other diseases mediated by an enzyme activity, e.g. Huntington's disease.
DC B04 B05
IN KARPUJ, M V; **STEINMAN, L**
PA (YEDA) YEDA RES & DEV CO LTD
CYC 86
PI WO 9965516 A1 19991223 (200013)* EN 61p A61K038-48
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9948239 A 20000105 (200024) A61K038-48
ADT WO 9965516 A1 WO 1999-US13615 19990617; AU 9948239 A AU 1999-48239 19990617
FDT AU 9948239 A Based on WO 9965516
PRAI US 1998-89603P 19980617
IC ICM A61K038-48
ICS A61K031-13
AB WO 9965516 A UPAB: 20000313
NOVELTY - Treatment of **transglutaminase** (T) mediated diseases involves administration of its inhibitor (TI).

ACTIVITY - Nootropic; antirheumatic; neuroprotective; antidiabetic; antiinflammatory. The antiinflammatory activity of a (TI), **monodansyl cadaverine** was tested using paraparetic mice with experimental autoimmune encephalomyelitis induced by injecting 4 mg of mouse spinal cord homogenate. 0.05 mM **monodansyl cadaverine** was injected intraperitoneally into one of two groups of mice after 13 days of disease induction. A significant influence (p=0.03 compared to control) of this inhibitor occured after the second day of injection and mice treated with the **monodansyl cadaverine** showed reversal in the paralytic disease.

MECHANISM OF ACTION - **Transglutaminase** inhibitor.

USE - The composition comprising (TI) is used in the treatment of (TI) mediated diseases like neurodegenerative diseases caused by aggregation of polyQ proteins, Huntington's disease, spinobulbar atrophy, spinocerebellar ataxia, dentatorubralpallidoluysian atrophy, cell mediated autoimmune disease like rheumatoid arthritis, multiple sclerosis or insulin dependent diabetes mellitus and other inflammatory diseases of the central nervous system (claimed).

ADVANTAGE - None given.

Dwg.0/7

FS CPI
FA AB; DCN
MC CPI: B04-E02; B04-E06; B04-F0400E; B04-F1100E; B14-C03; B14-C06; **B14-D06**; B14-E08; **B14-J01**; **B14-J01A**; **B14-J01A4**; **B14-S03**; B14-S04
TECH UPTX: 20000313

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: (TI) can also be presented as an antisense DNA of (T) gene or as DNA encoding it and is introduced into the cell of patient. The method of DNA introduction includes receptor mediated gene delivery, transkaryotic implantation, viral shuttle vectors, direct injection of non-infectious, non-oncogenic plasma DNA encapsulated in liposomes, immunoliposomes and a liposome/red blood cell membrane hybrid.

ABEX UPTX: 20000313

SPECIFIC COMPOUNDS - The specific (TI) compounds are **monodansyl cadaverine**, cystamine, putrescine, gamma-amino benzoic acid, N-benzyloxy carbonyl, 5-deazo-4-oxonorvaline p-nitrophenylester, glycine methyl ester, CuSO4, and tolbutamide (claimed).

ADMINISTRATION - Administration can be by any preferred route e.g. intraperitoneal, subcutaneous, oral routes and are given in dosages of 0.0001-100 mg/kg body weight daily.

L91 ANSWER 2 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN 1998-130408 [12] WPIX
DNC C1998-043052
TI Use of modulators of **trans glutaminase** activity - in promoting healing of wounds, chronic wounds and fibrotic disorders with reduced scarring.
DC B04 B05 D16
IN FERGUSON, M W J
PA (UYMA-N) UNIV VICTORIA MANCHESTER
CYC 72
PI WO 9804245 A1 19980205 (199812)* EN 30p A61K031-00
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
ZA 9606486 A 19980429 (199822)# 28p C12N000-00
AU 9666205 A 19980220 (199828) A61K031-00
ADT WO 9804245 A1 WO 1996-GB1785 19960725; ZA 9606486 A ZA 1996-6486 19960731; AU 9666205 A AU 1996-66205 19960725, WO 1996-GB1785 19960725

FDT AU 9666205 A Based on WO 9804245
PRAI WO 1996-GB1785 19960725; ZA 1996-6486 19960731
IC ICM A61K031-00; C12N000-00
ICS A61K031-13; A61K031-145; A61K031-18; A61K031-40; A61K038-12; C07C000-00
AB WO 9804245 A UPAB: 19980323
Use of an inhibitor of **transglutaminase** in promoting healing of wounds or fibrotic disorders with reduced scarring.
Also claimed is the use of a stimulator of **transglutaminase** activity in promoting healing of chronic wounds.
The **transglutaminase** is type II **transglutaminase**.
The inhibitor is an active site inhibitor or is a substrate competitive inhibitor. It is selected from cystamine, **monodansyl cadaverine**, 2-(3-(diallylamino) propionyl) benzothiophene, putrescine, bacitracin, a neutralising antibody (or an antigen-binding fragment of this specific to **transglutaminase**) or a derivative of 2((2-oxopropyl)thio) imidazolium. The neutralising antibody is an IgG antibody specific to **transglutaminase** and is a monoclonal antibody, polyclonal antibody or genetically engineered antibody.
USE - The **transglutaminase** inhibitor is used for promoting healing of wounds (e.g. skin wounds, tendon damage, crush injuries, eye wounds, central nervous system injuries or scar tissue formation resulting from strokes) or fibrotic disorders (e.g. pulmonary fibrosis, glomerulonephritis, liver cirrhosis or proliferative vitreo retinopathy). The **transglutaminase** stimulator may be used in treatment of chronic wounds (e.g. venous ulcers, diabetic ulcers or bed sores).
ADVANTAGE - The inhibitor/stimulator reduce scarring. Scar tissue formation provides mechanical strength to healed wounds but can be unsightly and may impair the function of the tissue. This is especially the case in the central nervous system.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C01; B04-G01; B04-L05; B06-H; B07-H; B14-N17B; D05-C03

L91 ANSWER 3 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN 1991-207851 [28] WPIX
DNC C1991-090106
TI Growth arrest of eukaryotic cells (e.g. B and T lymphocytes) - with the **trans-glutaminase** inhibitors **monodansyl cadaverine** or 1-(5-aminopentyl)-3-(phenylthiourea) useful as adjunct to chemotherapy.
DC B05
IN MEHTA, K; SAHASRABUDDHE, C G; SAHASRABUD, C G
PA (TEXA) UNIV TEXAS SYSTEM
CYC 30
PI WO 9108739 A 19910627 (199128)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL OA SE
W: AT AU BB BG CA CH DE DK ES FI GB GR HU JP KR LU MC MG MW NL NO RO SD SE SU
AU 9171618 A 19910718 (199142)
EP 505487 A1 19920930 (199240) EN 44p A61K031-17
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
JP 05502673 W 19930513 (199324) 11p A61K045-00
ADT EP 505487 A1 WO 1990-US7349 19901213, EP 1991-902418 19901213; JP 05502673 W WO 1990-US7349 19901213, JP 1991-502790 19901213
FDT EP 505487 A1 Based on WO 9108739; JP 05502673 W Based on WO 9108739
PRAI US 1989-451324 19891213
REP 6.Jnl.Ref
IC ICM A61K031-17; A61K045-00
ICS A61K031-18
AB WO 9108739 A UPAB: 19930928
The **transglutaminase** inhibitor is e.g. **monodansyl**

cadaverine (MDC), which may be used to arrest the growth of B lymphocytes, T lymphocytes or monocytes (in a cell cycle G1-phase). Another cpd. 1-(5-aminopentyl)-3-phenylthiourea (PPTU), is claimed for arresting B lymphocyte growth.

The inhibitors arrest the growth of normal and neoplastic B and T lymphocytes, preventing their entry into the S-phase of the cell cycle. The in vitro activity of MDC and PPTU indicate that these cpds. would be highly desirable adjunct to chemotherapy.

0/8

FS CPI
FA AB; DCN
MC CPI: B10-A08; B10-A13A; B12-G01B3; B12-G05; B12-G07
ABEQ JP 05502673 W UPAB: 19931116

The **transglutaminase** inhibitor is e.g. **monodansyl cadaverine** (MDC), which may be used to arrest the growth of B lymphocytes, T lymphocytes or monocytes (in a cell cycle G1-phase). Another cpd. 1-(5-aminopentyl)-3-phenylthiourea (PPTU), is claimed for arresting B lymphocyte growth.

The inhibitors arrest the growth of normal and neoplastic B and T lymphocytes, preventing their entry into the S-phase of the cell cycle. The in vitro activity of MDC and PPTU indicate that these cpds. would be highly desirable adjunct to chemotherapy.

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L1 1 S E3,E4
E WO9965516/PN
L2 1 S E3
L3 1 S L1,L2

FILE 'REGISTRY' ENTERED AT 15:26:23 ON 01 JUL 2003
L4 1 S 80146-85-6
L5 1 S 10121-91-2
L6 0 S 10121-91-2/CRN

FILE 'HCAPLUS' ENTERED AT 15:27:17 ON 01 JUL 2003
L7 265 S L5
L8 568 S DANSYLCADAVERIN# OR MONODANSYLCADAVERIN# OR (MONODANSYL OR DA
L9 6 S N 5 AMINOPENTYL 5 DIMETHYLAMINO 1 NAPHTHALENESULFONAMIDE
L10 617 S L7-L9
L11 538 S L10 AND (PD<=19980617 OR PRD<=19980617 OR AD<=19980617)
E STEINMAN L/AU
L12 208 S E3,E4
L13 1 S L10 AND L12
L14 1 S YEDA?/PA,CS AND L10
L15 1 S L3,L13,L14
L16 2799 S L4
L17 3813 S TRANSGLUTAMINASE OR TRANS GLUTAMINASE
L18 228 S L11 AND L16,L17
E HUNTINGTON/CT
E E5+ALL
E NERVOUS SYTEM/CT
E NERVOUS SYSTEM/CT
L19 3155 S NERVOUS SYSTEM/CT (L) (HUNTINGTON? OR CHOREA?)
E SPINOBULBAR/CT
E SPINOBULBAR
L20 85 S E2-E6

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L21          55 S L20 (L) ATROPH?
                E SPINOCEREBELLAR/CT
                E E4+ALL
L22         471 S E2
                E DENTATORUBRAL
L23         256 S E3-E8
                E BRAIN DISEASE/CT
                E E4+ALL
                E E2+ALL
L24         179 S E3-E5 (L) DENTATORUB?
L25         179 S E3-E5 (L) PALLIDOL?
L26           3 S L11 AND L19-L25
L27           3 S L11 AND (HUNTINGTON? OR CHOREA? OR SPINOBULBAR? OR SPINOCEREB
L28           3 S L26,L27 AND L18

     FILE 'REGISTRY' ENTERED AT 15:44:40 ON 01 JUL 2003
L29           5 S 51-85-4 OR 110-60-1 OR 64-77-7 OR 7758-98-7 OR 616-34-2
L30           2 S 150-13-0 OR 74389-76-7
L31         393 S 7664-93-9/CRN AND CU/ELS
L32          47 S L31 AND 2/NC
L33          44 S L32 NOT (CCS OR MXS OR IDS OR MNS OR PMS)/CI
L34          11 S L33 NOT ATO
L35           5 S L34 AND NR>=1
L36           6 S L34 NOT L35

     FILE 'HCAPLUS' ENTERED AT 15:50:38 ON 01 JUL 2003
L37       43274 S L29 OR L30 OR L36
L38         180 S L37 AND L16,L17
L39          15 S L37 AND L19-L25
L40          48 S L37 AND (HUNTINGTON? OR CHOREA? OR SPINOBULBAR? OR SPINOCEREB
L41           8 S L39,L40 AND L38
L42       37213 S L37 AND (PD<=19980617 OR PRD<=19980617 OR AD<=19980617)
L43         154 S L42 AND L38
L44          31 S L42 AND L39,L40
L45           4 S L43 AND L44
L46           5 S L28,L45
L47           3 S L12 AND L37
L48           7 S L46,L47
L49           1 S L11,L42 AND (POLYQ OR POLY Q)

     FILE 'REGISTRY' ENTERED AT 15:55:59 ON 01 JUL 2003
L50           2 S 24991-23-9 OR 25513-46-6
L51           4 S (5959-95-5 OR 6899-04-3)/CRN AND PMS/CI
L52           2 S L51 AND 1/NC
L53           1 S 101985-79-9
                E CAG
L54         194 S E3
L55           2 S L54 AND GUAN?

     FILE 'HCAPLUS' ENTERED AT 15:59:40 ON 01 JUL 2003
L56        2463 S L50,L52,L53
L57          19 S L56 AND L11,L42
L58           4 S L57 AND L16,L17
L59           3 S L58 NOT CLOTTING/TI
L60           7 S L48,L49,L59
L61           7 S L60 AND L1-L3,L7-L28,L37-L49,L56-L60

     FILE 'REGISTRY' ENTERED AT 16:02:56 ON 01 JUL 2003
L62           2 S 26700-71-0 OR 69864-43-3
L63         118 S (6893-26-1 OR 617-65-2)/CRN AND PMS/CI
L64           2 S L63 AND 1/NC

     FILE 'HCAPLUS' ENTERED AT 16:04:25 ON 01 JUL 2003
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L65          896 S L62,L64
L66          386 S L65 AND (PD<=19980617 OR PRD<=19980617 OR AD<=19980617)
L67            9 S L66 AND L16,L17
L68           64 S L66 AND L19-L25
L69            6 S L67 AND L68
L70           11 S L61,L69
L71           11 S L70 AND L1-L3,L7-L28,L37-L49,L56-L61,L65-L70

     FILE 'HCAPLUS' ENTERED AT 16:07:58 ON 01 JUL 2003
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 16:08:12 ON 01 JUL 2003
L72           14 S E1-E14

     FILE 'BIOSIS' ENTERED AT 16:08:28 ON 01 JUL 2003
L73          564 S L10
L74          470 S L73 AND PY<=1998
L75          209 S L74 AND L16,L17
L76            1 S L74 AND (HUNTINGTON? OR CHOREA? OR POLYQ OR POLY Q OR CAG OR
L77            1 S L74 AND L62,L64,L50,L52,L53
L78            1 S L76,L77
L79            1 S L75 AND L78
L80           16 S L74 AND (20506 OR 22024)/CC
L81            6 S L75,L79 AND L80
L82            7 S L79,L81
L83           10 S L80 NOT L82

     FILE 'BIOSIS' ENTERED AT 16:14:00 ON 01 JUL 2003

     FILE 'WPIX' ENTERED AT 16:14:19 ON 01 JUL 2003
L84           11 S L8/BIX OR L9/BIX
                 E DANSYLCADAVERINE/DCN
                 E DANSYL CADAVERINE/DCN
                 E CADAVERINE/DCN
                 E E3+ALL
                 E R21595+ALL/DCN
L85            5 S L84 AND (TRANSGLUTAMINASE OR TRANS GLUTAMINASE)/BIX
L86            1 S L84 AND (B14-D06 OR C14-D06 OR B12-G01B1 OR C12-G01B1)/MC
L87            1 S L84 AND (B14-J? OR C14-J? OR B12-C? OR C12-C?)/MC
L88            1 S L84 AND (B14-S03? OR C14-S03?)/MC
L89            1 S L84 AND STEINMAN L?/AU
L90            5 S L85-L89
L91            3 S L90 NOT (ZEBRAFISH OR NEMATODE)
L92            6 S L84 NOT L90

     FILE 'WPIX' ENTERED AT 16:21:20 ON 01 JUL 2003
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